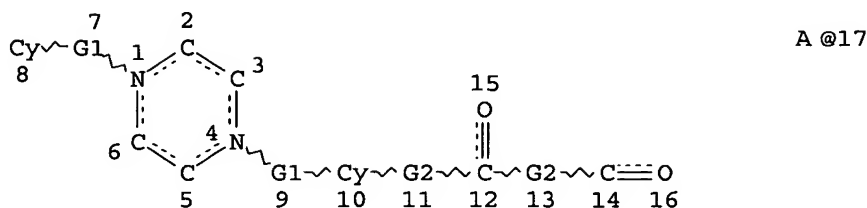


=&gt; d que 112

L1 379847 SEA FILE=REGISTRY ABB=ON PLU=ON NC2NC2/ES AND NRS>2 AND O>1  
 L6 STR



REP G1=(1-5) 17

REP G2=(0-5) 17

NODE ATTRIBUTES:

NSPEC IS RC AT 17

DEFAULT MLEVEL IS ATOM

GGCAT IS UNS AT 8

GGCAT IS UNS AT 10

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

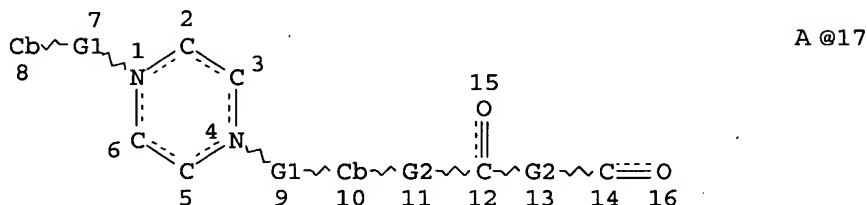
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

L9 766 SEA FILE=REGISTRY SUB=L1 SSS FUL L6

L10 STR



REP G1=(1-5) 17

REP G2=(0-5) 17

NODE ATTRIBUTES:

NSPEC IS RC AT 17

DEFAULT MLEVEL IS ATOM

GGCAT IS MCY UNS AT 8

GGCAT IS MCY UNS AT 10

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS E6 C AT 8

ECOUNT IS E6 C AT 10

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

L11 239 SEA FILE=REGISTRY SUB=L9 SSS FUL L10

L12 52 SEA FILE=HCAPLUS ABB=ON PLU=ON L11

=&gt; d 112 ibib abs hitstr 1-52

L12 ANSWER 1 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:182645 HCAPLUS

DOCUMENT NUMBER: 142:261563

TITLE: Preparation of phenylurea piperazine compounds as antitumor agents

INVENTOR(S): Drewry, David Harold; Mook, Robert Anthony, Jr.; Salovich, James Michael; Schoenen, Frank J.; Wagner, David S.; Wagner, Richard W.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019193	A2	20050303	WO 2004-US27418	20040817
WO 2005019193	A3	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

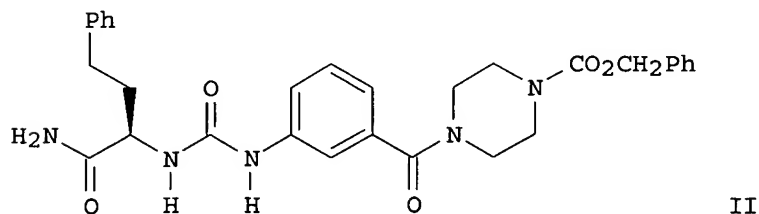
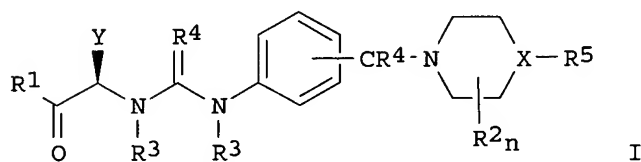
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-496488P

P 20030820

GI



AB Phenylurea compds. of formula I [R1 = (substituted) OH, (substituted) NH2; R2= halo, alkyl, etc.; n = 0-4; R3 = H, alkyl, cycloalkyl, etc.; R4 = O, S; R5 = H, alkyl, alkoxycarbonyl, absent, etc.; X = N, O, S, CH; Y = (substituted) phenylalkyl, heteroarylalkyl, etc.] are prepared for the

treatment of polo-like kinase mediated conditions such as neoplasms. Thus, II was prepared via solid-phase synthesis, and showed inhibitory activity against PLK1.

IT 846547-72-6P

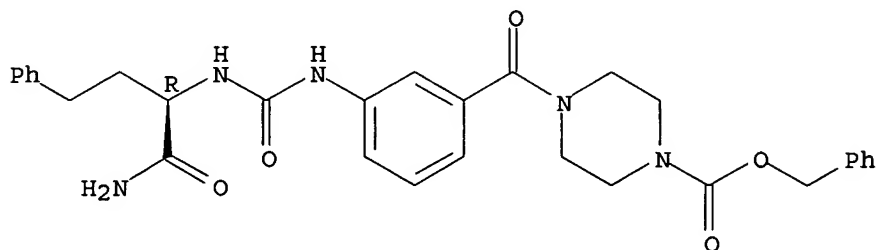
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of phenylurea piperazine compds. as antitumor agents)

RN 846547-72-6 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[3-[[[(1R)-1-(aminocarbonyl)-3-phenylpropyl]amino]carbonyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 2 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:931493 HCAPLUS

DOCUMENT NUMBER: 141:410707

TITLE: Preparation of malonic acids as protein tyrosine phosphatase (PTP) inhibitors and their pharmaceutical use

INVENTOR(S): Amanomiya, Yoshiya; Motoizumi, Masatoshi; Taniuchi, Makoto

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 166 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

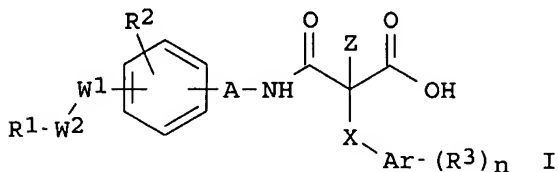
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004307460	A2	20041104	JP 2003-198893	20030718
PRIORITY APPLN. INFO.:			JP 2002-212121	A 20020722
			JP 2003-43056	A 20030220

OTHER SOURCE(S): MARPAT 141:410707

GI



AB Title compds. I [Ar = C6-10 aromatic; A = bond, CH<sub>2</sub>, C1-3 oxyalkylene; W1 = bond, oxyalkylene CO, O, CONH; W2 = bond, C<sub>6</sub>H<sub>4</sub>, C<sub>6</sub>H<sub>4</sub>O, C<sub>6</sub>H<sub>4</sub>CO, CH<sub>2</sub>CO; X = O, CH<sub>2</sub>; Z = H, F; R1 = C5-20 linear alkyl, C7-20 linear alkenyl, C7-20 linear alkadienyl, (un)substituted piperazinyl, (un)substituted Ph, etc; R2 = H, OH, O(CH<sub>2</sub>)<sub>na</sub>CO<sub>2</sub>H (na = 1-6); R2W1 may form ring; R3 = H, C1-6 alkyl, (CO<sub>2</sub>H-substituted) C1-6 alkoxy, CO<sub>2</sub>H; n = 1-3], useful for treatment of diabetes, obesity, hyperlipidemia, allergy, etc., are prepared Thus, amidation of 2-ethoxycarbonyl-3-phenylpropionic acid with 4-nitroaniline gave Et 2-(4-nitrophenylaminocarbonyl)-3-phenylpropionate, which was hydrogenated, amidated with palmitoyl chloride, and hydrolyzed to afford 2-[N-[4-(hexadecanoylamino)phenyl]aminocarbonyl]-3-phenylpropionic acid, which inhibited 92% human PTP-1B activity.

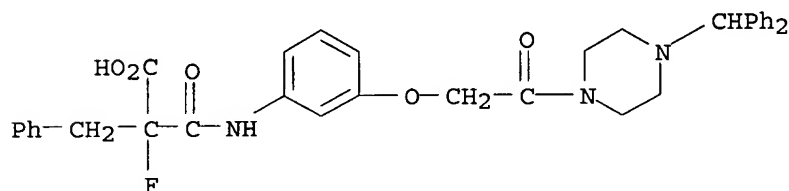
IT 790259-58-4P 790259-60-8P 790259-62-0P  
790259-64-2P 790259-66-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of malonic acids as protein tyrosine phosphatase inhibitors for treatment of diseases)

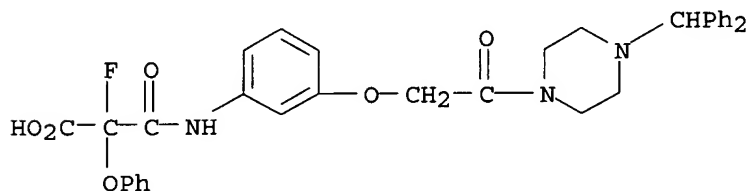
RN 790259-58-4 HCAPLUS

CN Benzenepropanoic acid, α-[[[3-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]-α-fluoro- (9CI) (CA INDEX NAME)



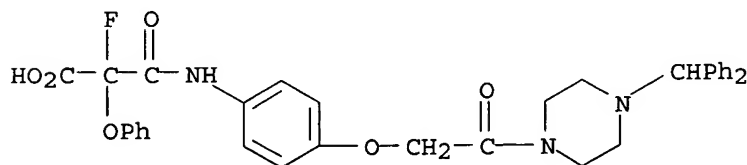
RN 790259-60-8 HCAPLUS

CN Propanoic acid, 3-[[[3-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-fluoro-3-oxo-2-phenoxy- (9CI) (CA INDEX NAME)



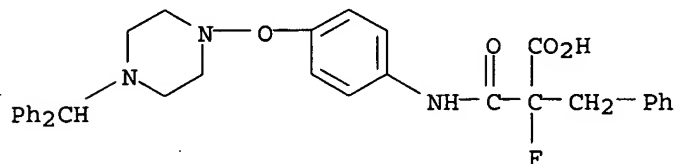
RN 790259-62-0 HCAPLUS

CN Propanoic acid, 3-[[[4-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-fluoro-3-oxo-2-phenoxy- (9CI) (CA INDEX NAME)



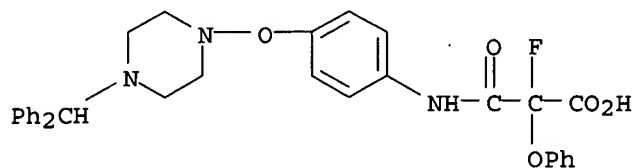


RN 790259-64-2 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -[[[4-[[4-(diphenylmethyl)-1-piperazinyl]oxy]phenyl]amino]carbonyl]- $\alpha$ -fluoro- (9CI) (CA INDEX NAME)

RN 790259-66-4 HCAPLUS

CN Propanoic acid, 3-[[4-[[4-(diphenylmethyl)-1-piperazinyl]oxy]phenyl]amino]-2-fluoro-3-oxo-2-phenoxy- (9CI) (CA INDEX NAME)

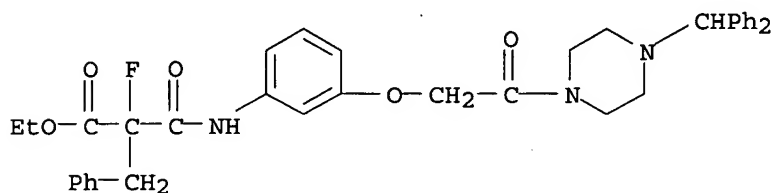


IT 790262-45-2P 790262-46-3P 790262-48-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

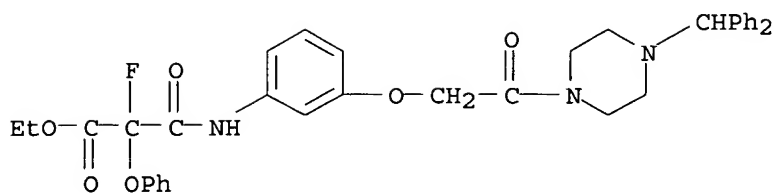
(preparation of malonic acids as protein tyrosine phosphatase inhibitors for treatment of diseases)

RN 790262-45-2 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -[[[3-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- $\alpha$ -fluoro-, ethyl ester (9CI) (CA INDEX NAME)

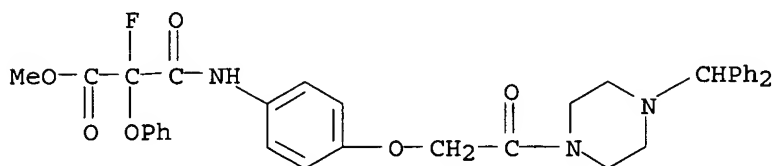
RN 790262-46-3 HCAPLUS

CN Propanoic acid, 3-[[3-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-fluoro-3-oxo-2-phenoxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 790262-48-5 HCAPLUS

CN Propanoic acid, 3-[[4-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-fluoro-3-oxo-2-phenoxy-, methyl ester (9CI) (CA INDEX NAME)



L12 ANSWER 3 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:753392 HCAPLUS

DOCUMENT NUMBER: 141:260408

TITLE: Preparation of 3-amino-2-hydroxy-4-phenylbutyric acid as protein tyrosin phosphatase inhibitors

INVENTOR(S): Amanomiya, Yoshiya; Taniuchi, Makoto

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 69 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

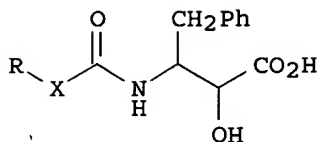
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

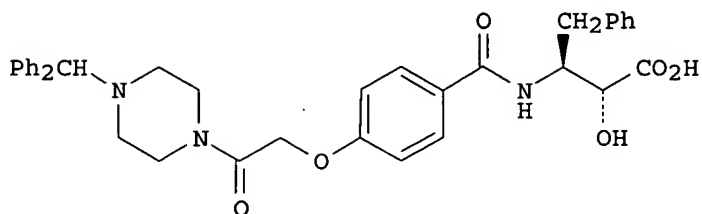
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004256435	A2	20040916	JP 2003-48605	20030226
PRIORITY APPLN. INFO.:			JP 2003-48605	20030226
OTHER SOURCE(S):	MARPAT	141:260408		

GI



I



II

AB Title compds. represented by the formula I [wherein X = single bond or (un)substituted arylene; R = (un)substituted alkyl, alkoxy, alkylamino; and pharmaceutically acceptable salts or esters thereof] were prepared as protein tyrosin phosphatase inhibitors. For example, II was given in a multi-step synthesis starting from the reaction of Me 4-hydroxybenzoate with tert-Bu bromoacetate. I showed inhibition of the protein tyrosin phosphatase with 26-101% blocking rate, and their formulations also were presented. Thus, I and their pharmaceutical compns. are useful as protein tyrosin phosphatase inhibitors.

IT 756823-00-4P 756823-01-5P 756823-02-6P  
756823-03-7P 756823-17-3P 756823-18-4P  
756823-19-5P

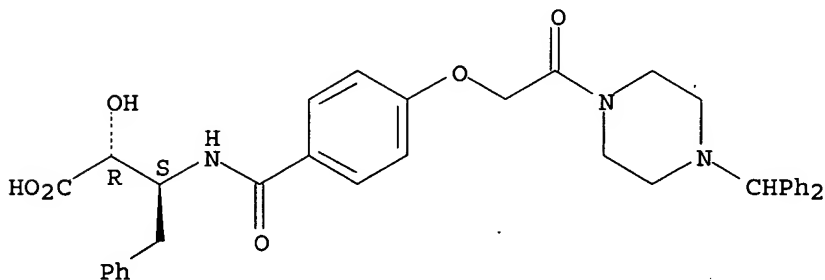
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3-amino-2-hydroxy-4-phenylbutyric acids as protein tyrosin phosphatase inhibitors)

RN 756823-00-4 HCAPLUS

CN Benzenebutanoic acid,  $\beta$ -[[4-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]benzoyl]amino]- $\alpha$ -hydroxy-, ( $\alpha$ R, $\beta$ S)-rel- (9CI)  
(CA INDEX NAME)

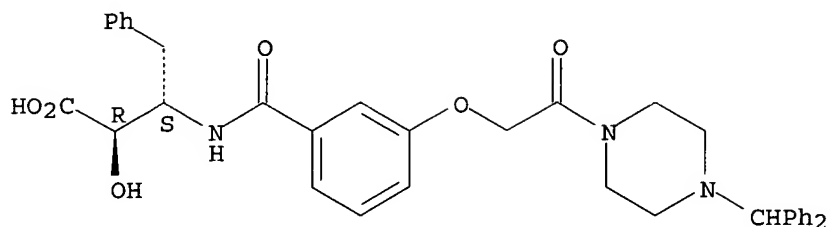
Relative stereochemistry.



RN 756823-01-5 HCAPLUS

CN Benzenebutanoic acid,  $\beta$ -[[3-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]benzoyl]amino]- $\alpha$ -hydroxy-, ( $\alpha$ R, $\beta$ S)-rel- (9CI)  
(CA INDEX NAME)

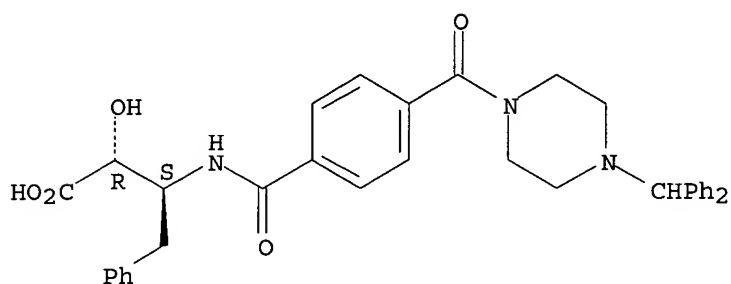
Relative stereochemistry.



RN 756823-02-6 HCAPLUS

CN Benzenebutanoic acid,  $\beta$ -[[4-[[4-(diphenylmethyl)-1-piperazinyl]carbonyl]benzoyl]amino]- $\alpha$ -hydroxy-, ( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

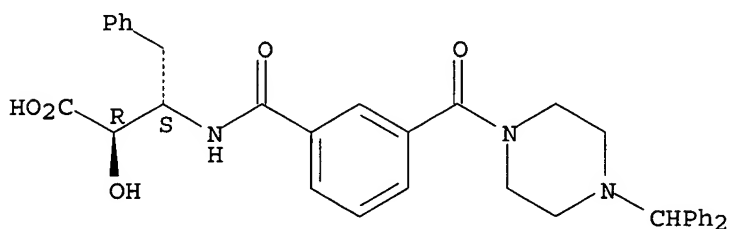
Relative stereochemistry.



RN 756823-03-7 HCAPLUS

CN Benzenebutanoic acid,  $\beta$ -[[3-[[4-(diphenylmethyl)-1-piperazinyl]carbonyl]benzoyl]amino]- $\alpha$ -hydroxy-, ( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

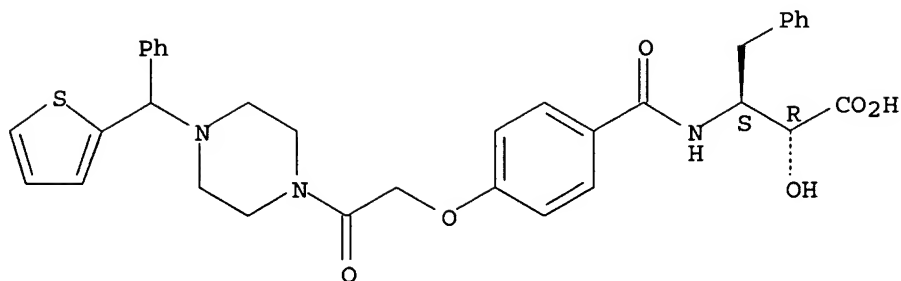
Relative stereochemistry.



RN 756823-17-3 HCAPLUS

CN Benzenebutanoic acid,  $\alpha$ -hydroxy- $\beta$ -[[4-[2-oxo-2-[4-(phenyl-2-thienylmethyl)-1-piperazinyl]ethoxy]benzoyl]amino]-, ( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

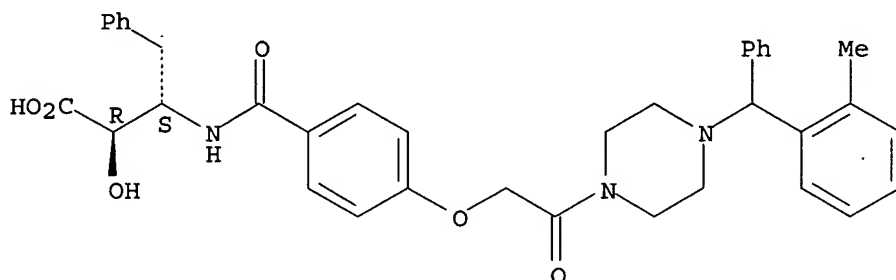
Relative stereochemistry.



RN 756823-18-4 HCAPLUS

CN Benzenebutanoic acid,  $\alpha$ -hydroxy- $\beta$ -[[4-[2-[4-[(2-methylphenyl)phenylmethyl]-1-piperazinyl]-2-oxoethoxy]benzoyl]amino]-, ( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

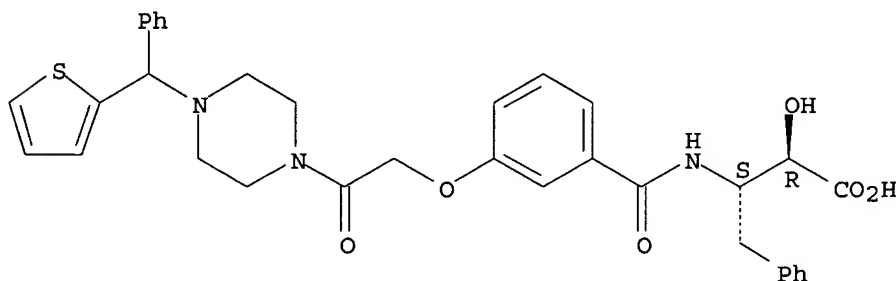
Relative stereochemistry.



RN 756823-19-5 HCAPLUS

CN Benzenebutanoic acid,  $\alpha$ -hydroxy- $\beta$ -[[3-[2-oxo-2-[4-(phenyl-2-thienylmethyl)-1-piperazinyl]ethoxy]benzoyl]amino]-, ( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 756823-25-3P 756823-28-6P 756823-31-1P

756823-34-4P 756823-69-5P 756823-73-1P

756823-76-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

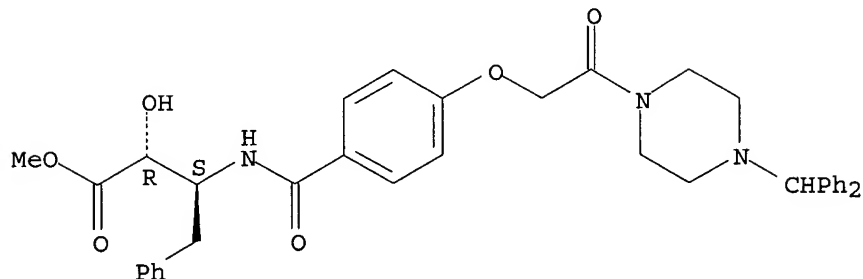
(preparation of 3-amino-2-hydroxy-4-phenylbutyric acids as protein tyrosin phosphatase inhibitors)

RN 756823-25-3 HCAPLUS

CN Benzenebutanoic acid,  $\beta$ -[[4-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-

oxoethoxy]benzoyl]amino]- $\alpha$ -hydroxy-, methyl ester,  
( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

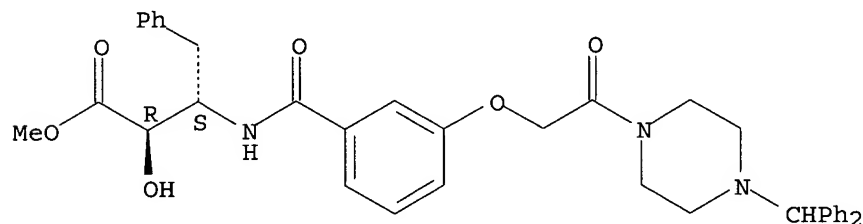
Relative stereochemistry.



RN 756823-28-6 HCAPLUS

CN Benzenebutanoic acid,  $\beta$ -[[3-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]benzoyl]amino]- $\alpha$ -hydroxy-, methyl ester,  
( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

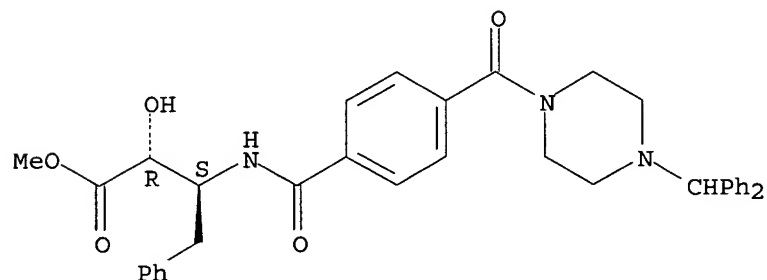
Relative stereochemistry.



RN 756823-31-1 HCAPLUS

CN Benzenebutanoic acid,  $\beta$ -[[4-[[4-(diphenylmethyl)-1-piperazinyl]carbonyl]benzoyl]amino]- $\alpha$ -hydroxy-, methyl ester,  
( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

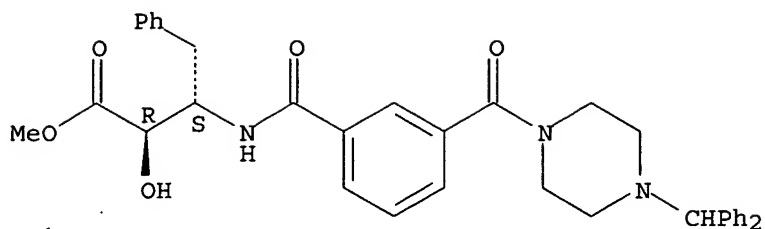
Relative stereochemistry.



RN 756823-34-4 HCAPLUS

CN Benzenebutanoic acid,  $\beta$ -[[3-[[4-(diphenylmethyl)-1-piperazinyl]carbonyl]benzoyl]amino]- $\alpha$ -hydroxy-, methyl ester,  
( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

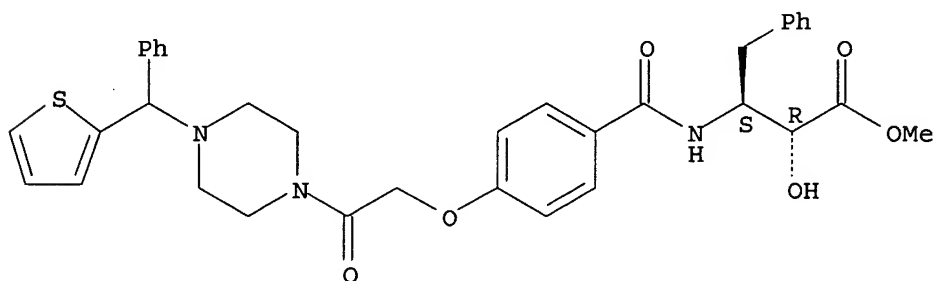
Relative stereochemistry.



RN 756823-69-5 HCAPLUS

CN Benzenebutanoic acid,  $\alpha$ -hydroxy- $\beta$ -[[4-[2-oxo-2-[4-(phenyl-2-thienylmethyl)-1-piperazinyl]ethoxy]benzoyl]amino]-, methyl ester, ( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

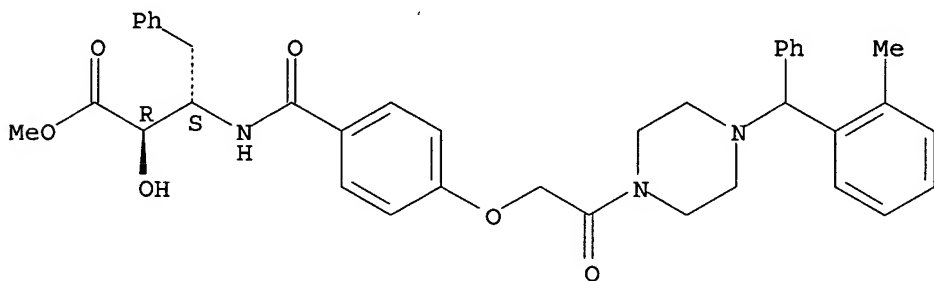
Relative stereochemistry.



RN 756823-73-1 HCAPLUS

CN Benzenebutanoic acid,  $\alpha$ -hydroxy- $\beta$ -[[[4-[2-[4-[(2-methylphenyl)phenylmethyl]-1-piperazinyl]-2-oxoethoxy]benzoyl]amino]-, methyl ester, ( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

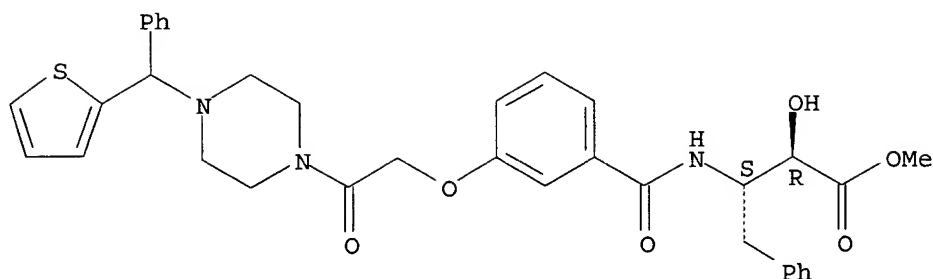
Relative stereochemistry.



RN 756823-76-4 HCAPLUS

CN Benzenebutanoic acid,  $\alpha$ -hydroxy- $\beta$ -[[3-[2-oxo-2-[4-(phenyl-2-thienylmethyl)-1-piperazinyl]ethoxy]benzoyl]amino]-, methyl ester, ( $\alpha$ R, $\beta$ S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 4 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:392321 HCAPLUS

DOCUMENT NUMBER: 140:406826

TITLE: Preparation of N-benzylpiperazine derivatives as chemokine receptor CCR1 antagonists useful as immunomodulatory agents

INVENTOR(S): Blumberg, Laura C.; Brown, Matthew F.; Gaweco, Anderson S.; Gladue, Ronald P.; Hayward, Matthew M.; Lundquist, Gregory D.; Poss, Christopher S.; Shavnya, Andrei

PATENT ASSIGNEE(S): Pfizer Inc, USA

SOURCE: U.S. Pat. Appl. Publ., 58 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

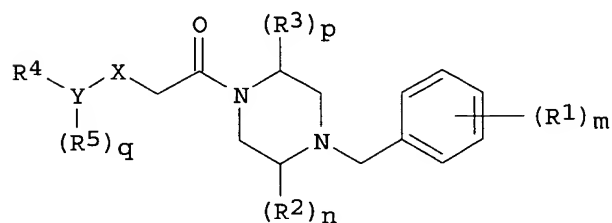
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092529	A1	20040513	US 2003-686993	20031016
PRIORITY APPLN. INFO.:			US 2002-422590P	P 20021030
OTHER SOURCE(S):	MARPAT	140:406826		

GI



I

AB The present invention relates to compds. of the formula (I) and the pharmaceutically acceptable forms thereof [m = 0-5; n, p = 0-2; q = 0-4; X = O, S, CH<sub>2</sub>, (un)substituted NH; Y = C<sub>6</sub>-10 aryl, C<sub>2</sub>-9 heteroaryl; R<sub>1</sub> = H, HO, halo, C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkoxy, HO-C<sub>1</sub>-8 alkyl, cyano, NH<sub>2</sub>, H<sub>2</sub>N-C<sub>1</sub>-8 alkyl, CO<sub>2</sub>H, C<sub>1</sub>-8 alkyl-CO, C<sub>1</sub>-8 alkyl-CO-C<sub>1</sub>-8 alkyl, CONH<sub>2</sub>, or H<sub>2</sub>NCO-C<sub>1</sub>-8 alkyl; R<sub>2</sub>, R<sub>3</sub> = H, oxo, C<sub>1</sub>-8 alkyl, C<sub>3</sub>-8 cycloalkyl-C<sub>1</sub>-8 alkyl, C<sub>6</sub>-10 aryl, C<sub>6</sub>-10 aryl-C<sub>1</sub>-8 alkyl, HO-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-O-C<sub>1</sub>-8 alkyl, H<sub>2</sub>N-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-NH-C<sub>1</sub>-8 alkyl, (C<sub>1</sub>-8 alkyl)<sub>2</sub>N-C<sub>1</sub>-8 alkyl, C<sub>2</sub>-9 heterocyclyl-C<sub>1</sub>-8 alkyl, C<sub>3</sub>-8 cycloalkyl-NH-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8



alkyl-CO-NH-C1-8 alkyl-O-CO-NH-C1-8 alkyl, H<sub>2</sub>NCO-NH-C1-8 alkyl, C1-8 alkyl-SO<sub>2</sub>NH-C1-8 alkyl, C2-9 heteroaryl-C1-8 alkyl, H<sub>2</sub>NCO, H<sub>2</sub>NCO-C1-8 alkyl; R<sub>4</sub> = (HO<sub>2</sub>C)(H<sub>2</sub>N)-C1-8 alkyl, (HO<sub>2</sub>C)[(C1-8 alkyl)NH]-C1-8 alkyl, (HO<sub>2</sub>C)[(C1-8 alkyl)N]-C1-8 alkyl, (HO<sub>2</sub>C-C1-8 alkyl)(C1-8 alkyl)N, (HO<sub>2</sub>C-C1-8 alkyl)(C1-8 alkyl)N-C1-8 alkyl, (HO<sub>2</sub>C-C1-8 alkyl)(C1-8 alkyl-SO<sub>2</sub>)N, (HO<sub>2</sub>C-C1-8 alkyl)(C1-8 alkyl-SO<sub>2</sub>)N-C1-8 alkyl, (HO<sub>2</sub>C-C1-8 alkyl)(C1-8 alkyl-CO)N, etc.; R<sub>5</sub> = H, HO, halo, cyano, CO<sub>2</sub>H, H<sub>2</sub>N, C1-8 alkyl-NH, (C1-8 alkyl)<sub>2</sub>N, C1-8 alkyl, C1-8 alkyl-O, HO-C1-8 alkyl, C1-8 alkyl-NH-C1-8 alkyl, (C1-8 alkyl)<sub>2</sub>N-C1-8 alkyl, etc.]. Moreover, the present invention is also directed at pharmaceutical compns. comprising the compound I and a pharmaceutically acceptable carrier. Furthermore, the present invention is directed at methods of using the herein described compds. and compns. for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal. Particularly, disclosed is a method of treating or preventing a disorder or condition selected from the group consisting of fibrosis, Alzheimer's disease, conditions associated with leptin production, sequelae associated with cancer, cancer metastasis, diseases or conditions related to production of cytokines at inflammatory sites, and tissue damage caused by inflammation induced by infectious agents, wherein the method comprises administering to a mammal in need of such treatment or prevention a pharmaceutically effective amount of the compound I or a pharmaceutically acceptable form thereof. The compds. I are potent and selective inhibitors of MIP-1 $\alpha$  (CCL3) binding to its receptor CCR1 found on inflammatory and immunomodulatory cells (preferably leukocytes and lymphocytes). [2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methylphenoxy]acetic acid was condensed with methanesulfonamide in CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 18 h using 4-dimethylaminopyridine and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride to give N-[[2-[3-[4-(4-fluoro-benzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxo-propyl]-5-methylphenoxy]acetyl]methanesulfonamide. All the compds. I inhibited MIP-1 $\alpha$  (and the related chemokines shown to interact with CCR1) induced chemotaxis of THP-1 cells and human leukocytes with IC<sub>50</sub> of <10  $\mu$ M.

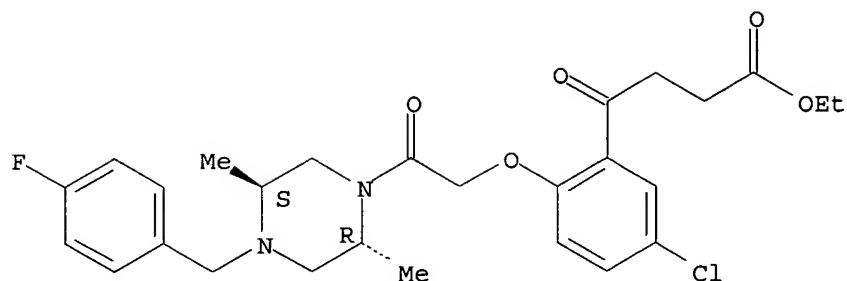
IT 519171-88-1P, 4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-4-Oxo-Butyric acid Ethyl Ester 519171-91-6P, 3-[3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Ureido]-Propionic acid Methyl Ester 519172-23-7P, Acetic acid 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzenesulfonylamino]-1,1-Dimethyl-2-Oxo-Ethyl Ester 519172-31-7P, Acetic acid 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenylmethanesulfonylamino]-1,1-Dimethyl-2-Oxo-Ethyl Ester 519172-93-1P, 5-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-5-Oxo-Pentanoic acid Ethyl Ester  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

RN 519171-88-1 HCAPLUS

CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]- $\gamma$ -oxo-, ethyl ester (9CI)  
(CA INDEX NAME)

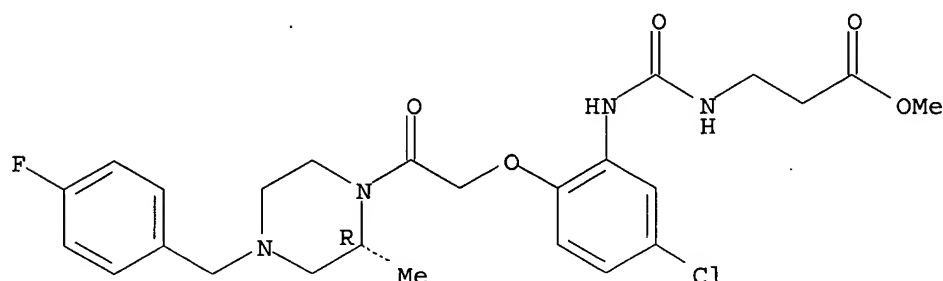
Absolute stereochemistry.



RN 519171-91-6 HCAPLUS

CN     $\beta$ -Alanine, N-[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

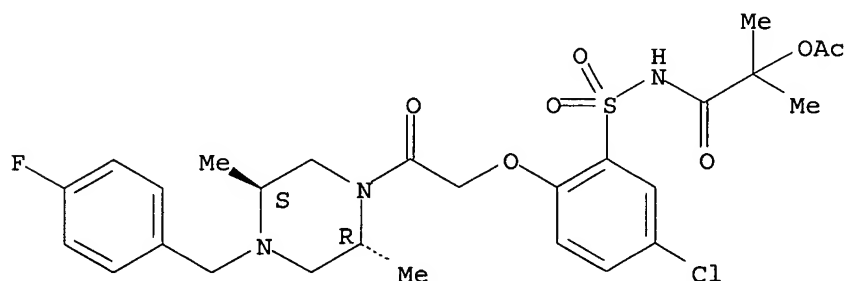
Absolute stereochemistry.



RN 519172-23-7 HCAPLUS

CN Propanamide, 2-(acetyloxy)-N-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]sulfonyl]-2-methyl- (9CI) (CA INDEX NAME)

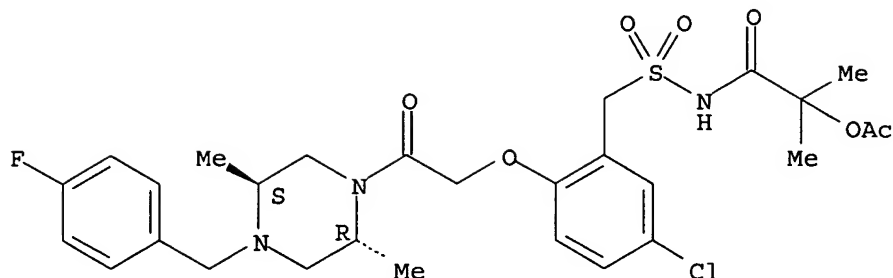
Absolute stereochemistry.



RN 519172-31-7 HCAPLUS

CN Propanamide, 2-(acetyloxy)-N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]sulfonyl]-2-methyl- (9CI) (CA INDEX NAME)

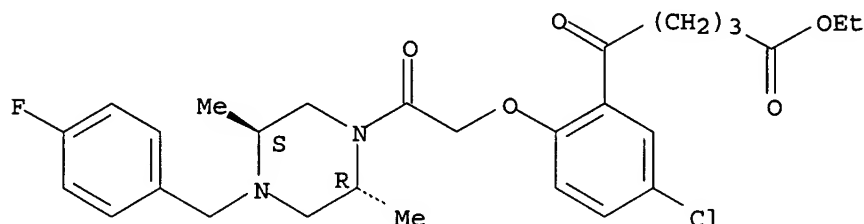
Absolute stereochemistry.



RN 519172-93-1 HCAPLUS

CN Benzenepentanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-8-oxo-, ethyl ester (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

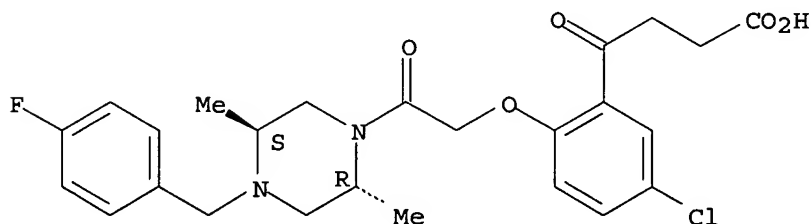


IT 519171-87-0P, 4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-4-Oxo-Butyric Acid  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

RN 519171-87-0 HCAPLUS

CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-γ-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 519172-90-8P, 5-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-5-Oxo-Pentanoic Acid  
519173-17-2P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-oxoacetic acid  
519173-72-9P, [3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]acetic acid

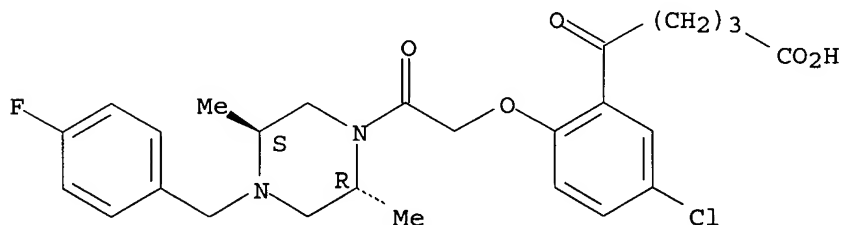
519173-73-0P, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid  
 519173-74-1P, 3-[3-[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid  
 519173-75-2P, [3-[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]acetic acid  
 519174-44-8P, [[[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]sulfonyl]amino]-oxoacetic acid  
 519174-74-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonylamino]-oxoacetic acid  
 519174-76-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonylamino]-oxoacetic acid  
 519175-34-9P, 3-[3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Ureido]-Propionic Acid  
 519175-35-0P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-oxobutyric acid  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

RN 519172-90-8 HCAPLUS

CN Benzenepentanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-8-oxo- (9CI) (CA INDEX NAME)

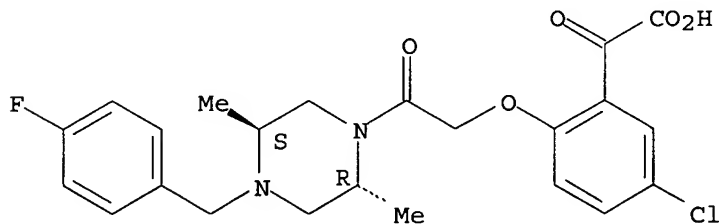
Absolute stereochemistry.



RN 519173-17-2 HCAPLUS

CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-α-oxo- (9CI) (CA INDEX NAME)

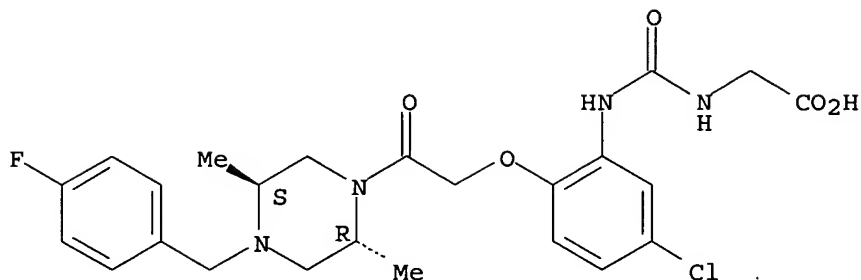
Absolute stereochemistry.



RN 519173-72-9 HCAPLUS

CN Glycine, N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

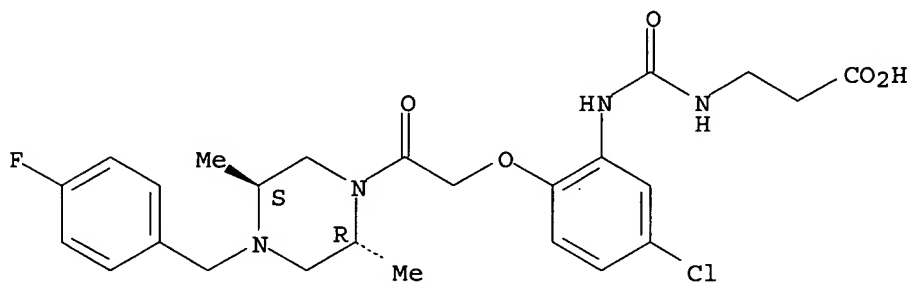
Absolute stereochemistry.



RN 519173-73-0 HCAPLUS

CN  $\beta$ -Alanine, N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl] - (9CI) (CA INDEX NAME)

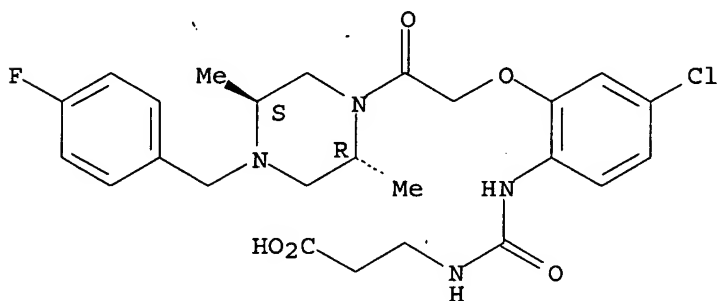
Absolute stereochemistry.



RN 519173-74-1 HCAPLUS

CN  $\beta$ -Alanine, N-[[[4-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl] - (9CI) (CA INDEX NAME)

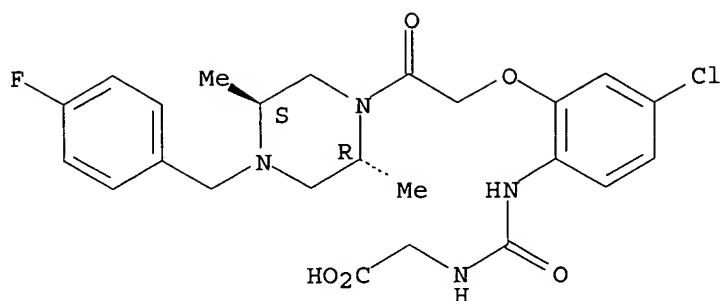
Absolute stereochemistry.



RN 519173-75-2 HCAPLUS

CN Glycine, N-[[[4-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl] - (9CI) (CA INDEX NAME)

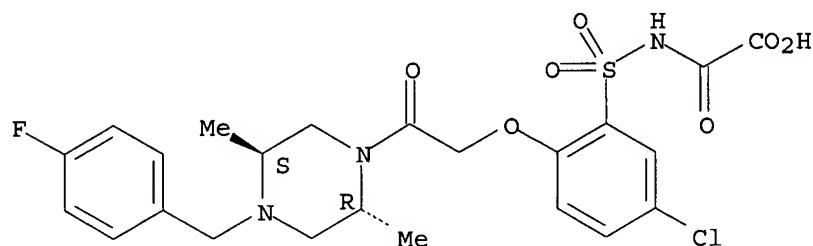
Absolute stereochemistry.



RN 519174-44-8 HCAPLUS

CN Acetic acid, [[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

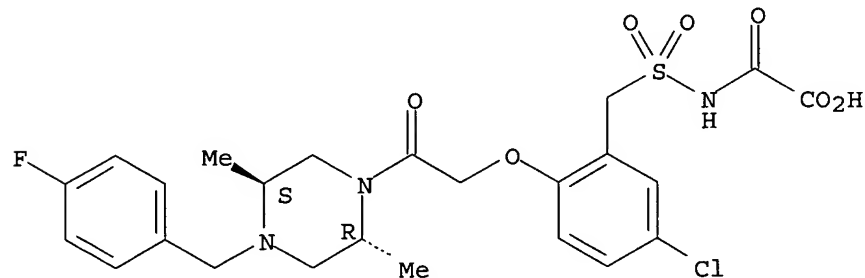
Absolute stereochemistry.



RN 519174-74-4 HCAPLUS

CN Acetic acid, [[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

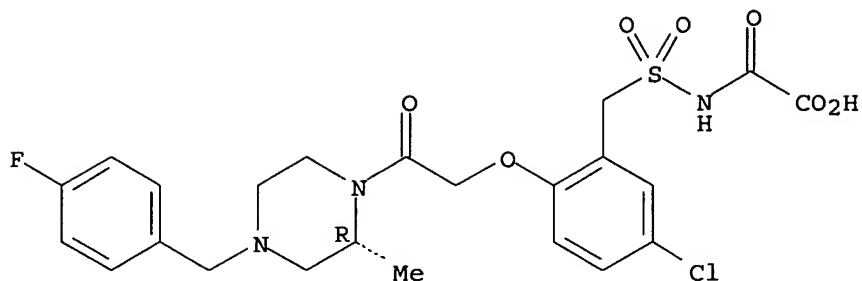
Absolute stereochemistry.



RN 519174-76-6 HCAPLUS

CN Acetic acid, [[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

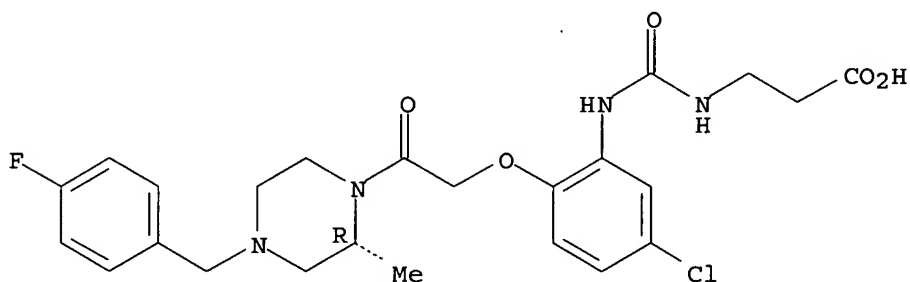
Absolute stereochemistry.



RN 519175-34-9 HCAPLUS

CN  $\beta$ -Alanine, N-[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

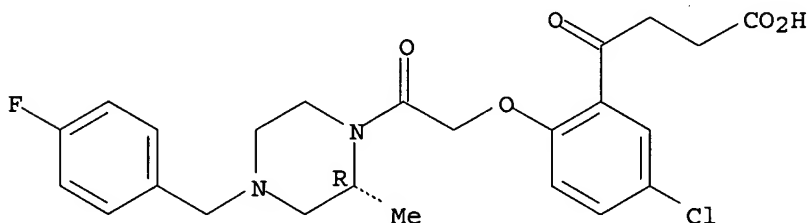
Absolute stereochemistry.



RN 519175-35-0 HCAPLUS

CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]- $\gamma$ -oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 5 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:387265 HCAPLUS

DOCUMENT NUMBER: 140:391297

TITLE: Preparation of piperazine derivatives as CCR1 antagonists

INVENTOR(S): Blumberg, Laura Cook; Brown, Matthew Frank; Gaweco, Anderson See; Gladue, Ronald Paul; Hayward, Matthew Merrill; Lundquist, Gregory Dean; Poss, Christopher Stanley; Shavnya, Andre

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 131 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

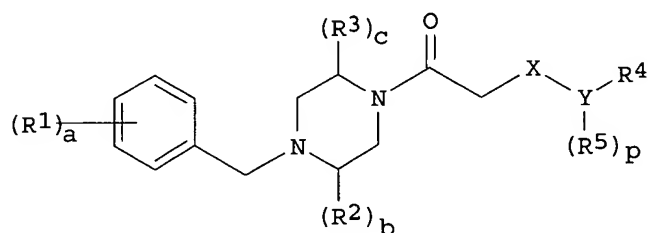
FAMILY ACC. NUM. COUNT:

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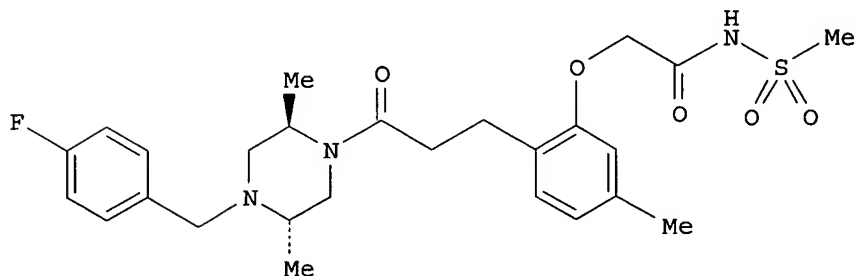
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039376	A1	20040513	WO 2003-IB4612	20031020
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2002-422590P	P 20021030
OTHER SOURCE(S):		MARPAT 140:391297		

GI



I



II

AB Title compds. I [a = 0-5; b,c = 0-2; p = 0-4; X = O, S, CH<sub>2</sub>, (un)substituted amino; Y = (hetero)aryl; R<sub>1</sub> = H, OH, halo, alkyl, alkoxy, etc.; R<sub>2-3</sub> = H, oxo, (cyclo)alkyl, aryl, etc.; R<sub>4</sub> = alkyl, etc.; R<sub>5</sub> = H, OH, halo, CN, etc.] are prepared For instance, (2R,5S)-1-(4-fluorobenzyl)-2,5-dimethylpiperazine (preparation given) is reacted with 7-methylchroman-2-



one (PhMe, reflux 48 h), the resulting propanone treated with bromoacetic acid Me ester (THF, NaH) and the ester saponified to give II. All example compds. have IC50 < 10 µM in the chemotaxis assay. I are useful for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal.

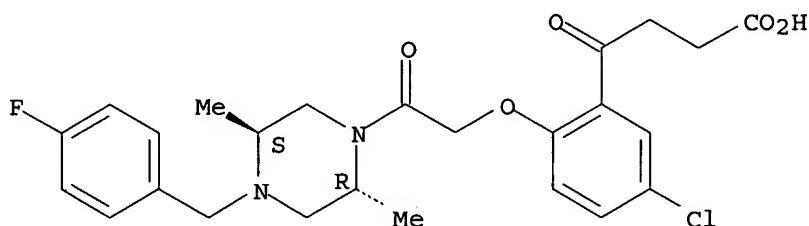
IT 519171-87-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

RN 519171-87-0 HCAPLUS

CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-γ-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 519172-90-8P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-oxopentanoic acid

519173-17-2P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]oxoacetic acid

519173-72-9P 519173-73-0P 519173-74-1P

519173-75-2P 519174-44-8P 519174-74-4P,

[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonylamino]oxoacetic acid 519174-76-6P

, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonylamino]oxoacetic acid 519175-35-0P

, (R)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-oxobutanoic acid 688031-94-9P,

(R)-3-[N'-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid hydrochloride

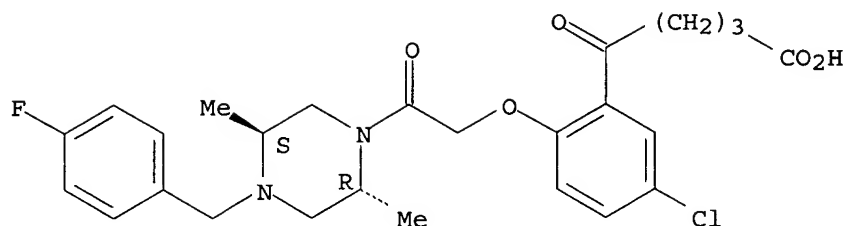
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

RN 519172-90-8 HCAPLUS

CN Benzenepentanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-δ-oxo- (9CI) (CA INDEX NAME)

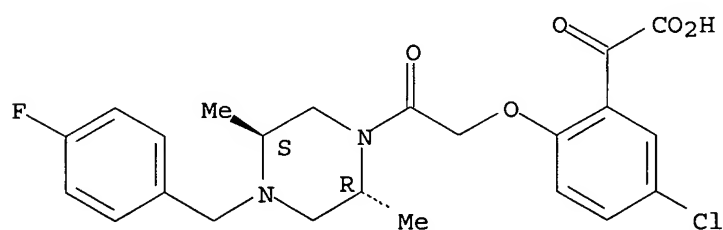
Absolute stereochemistry.



RN 519173-17-2 HCAPLUS

CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-α-oxo- (9CI) (CA INDEX NAME)

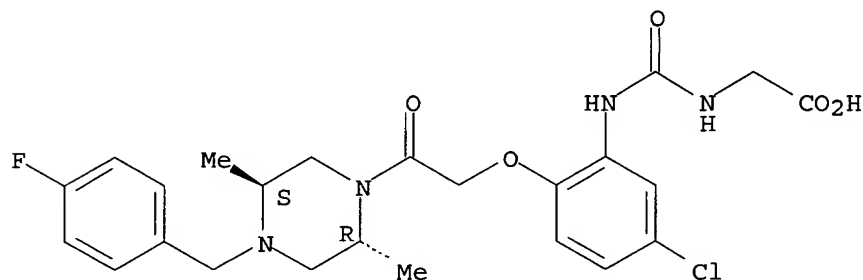
Absolute stereochemistry.



RN 519173-72-9 HCAPLUS

CN Glycine, N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

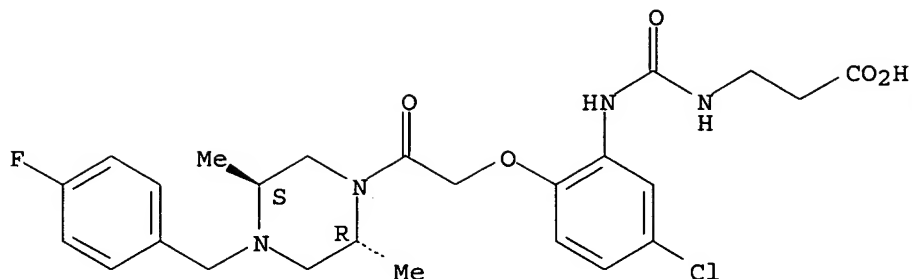
Absolute stereochemistry.



RN 519173-73-0 HCAPLUS

CN β-Alanine, N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

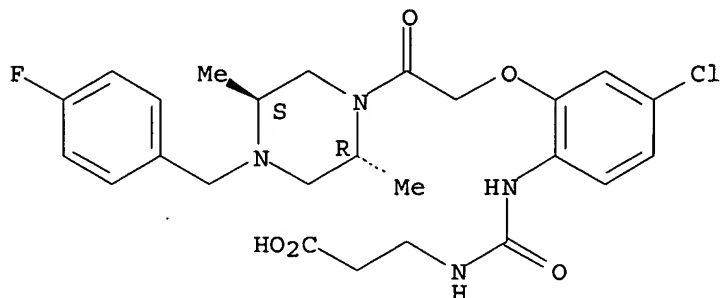
Absolute stereochemistry.



RN 519173-74-1 HCAPLUS

CN  $\beta$ -Alanine, N-[[[4-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

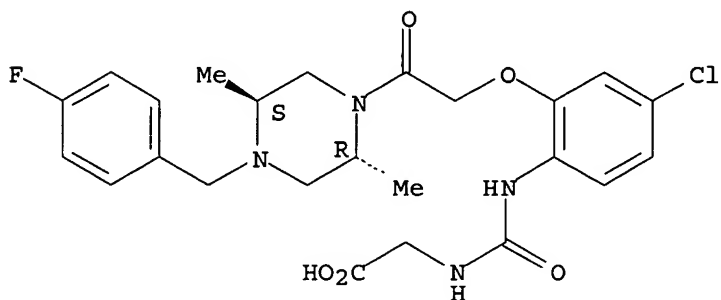
Absolute stereochemistry.



RN 519173-75-2 HCAPLUS

CN Glycine, N-[[[4-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

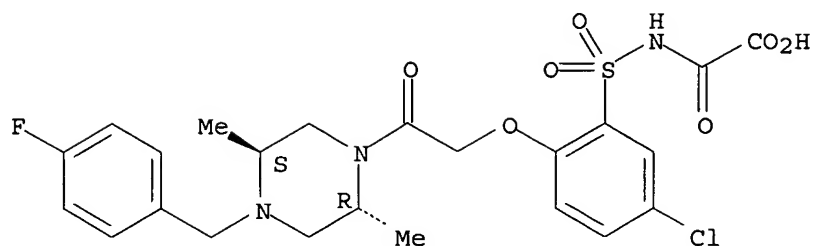
Absolute stereochemistry.



RN 519174-44-8 HCAPLUS

CN Acetic acid, [[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

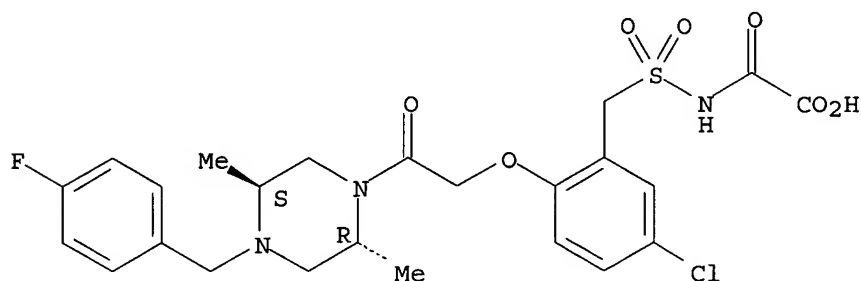
Absolute stereochemistry.



RN 519174-74-4 HCAPLUS

CN Acetic acid, [[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl)methyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

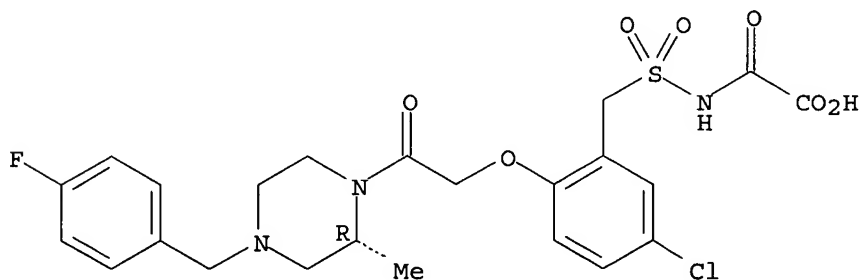
Absolute stereochemistry.



RN 519174-76-6 HCAPLUS

CN Acetic acid, [[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl)methyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

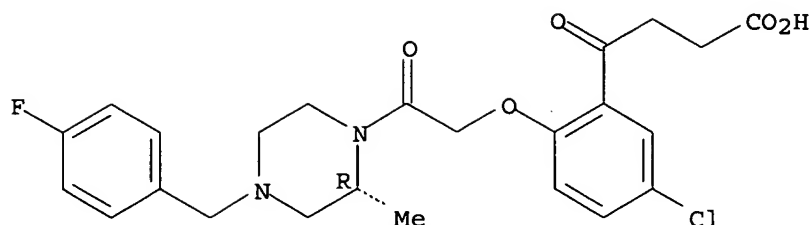
Absolute stereochemistry.



RN 519175-35-0 HCAPLUS

CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]-gamma-oxo- (9CI) (CA INDEX NAME)

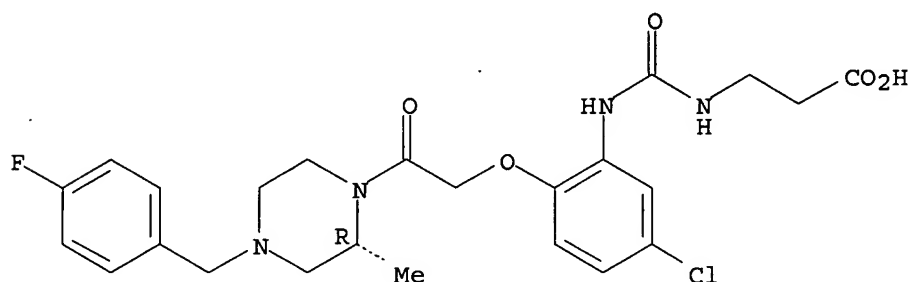
Absolute stereochemistry.



RN 688031-94-9 HCAPLUS

CN  $\beta$ -Alanine, N-[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

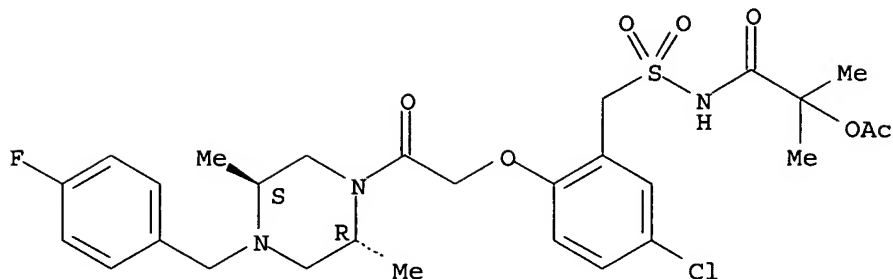
IT 519171-88-1P 519171-91-6P, (R)-3-[N'-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid methyl ester 519172-23-7P, Acetic acid 2-[[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzene]sulfonyl]amino]-1,1-dimethyl-2-oxoethyl ester 519172-31-7P, Acetic acid 2-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonyl]amino]-1,1-dimethyl-2-oxoethyl ester 519172-93-1P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-oxopentanoic acid ethyl ester  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

RN 519171-88-1 HCAPLUS

CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]- $\gamma$ -oxo-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

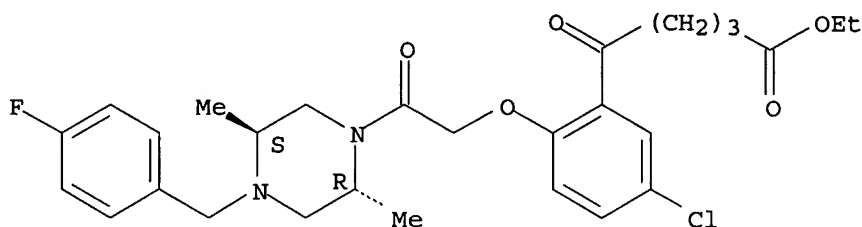




RN 519172-93-1 HCAPLUS

CN Benzenepentanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-8-oxo-, ethyl ester (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 6 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:719439 HCAPLUS

DOCUMENT NUMBER: 139:245783

TITLE: Preparation of arylamidine derivatives as fungicides

INVENTOR(S): Hayashi, Kazuya; Ojima, Katsuji; Hori, Kozo; Okujo, Hiroyuki; Mitsuyama, Junichi; Kunitani, Kazuto; Tohdo, Keisuke

PATENT ASSIGNEE(S): Toyama Chemical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 173 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

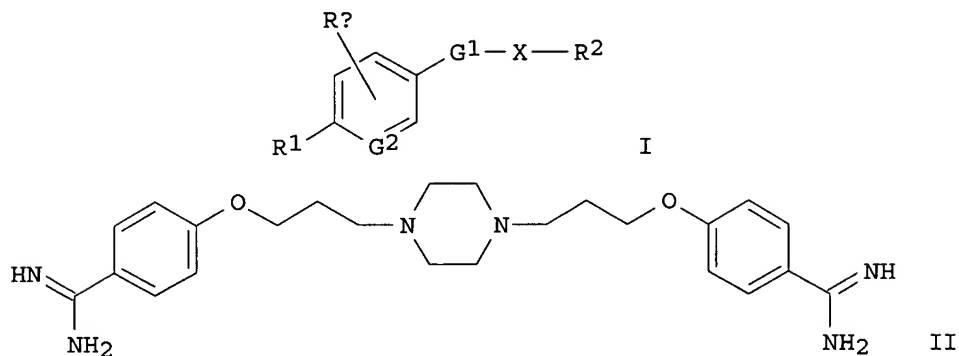
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074476	A1	20030912	WO 2003-JP2506	20030304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2477212	AA	20030912	CA 2003-2477212	20030304

EP 1481966 A1 20041201 EP 2003-743600 20030304  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
BR 2003008207 A 20041221 BR 2003-8207 20030304  
PRIORITY APPLN. INFO.: JP 2002-60618 A 20020306  
WO 2003-JP2506 W 20030304  
OTHER SOURCE(S): MARPAT 139:245783  
GI



AB The title arylamidine derivs. with general formula of I [wherein X = (un)substituted alkylene or alkenylene; G1 = O, S, or imino; G2 = CH or N; Ra = H, halo, (un)substituted alkyl, cycloalkyl, or alkoxy; R1 = (un)substituted amidino; R2 = (un)substituted NH2, etc.] and salts thereof are prepared as fungicides. For example, the compound II•xHCl was prepared in a multi-step synthesis. II showed IC50 of 0.0039 µg/mL against synthetic amino acid medium fungal (SAAMF) in agar.

IT 596809-41-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of arylamidine derivs. as fungicides)

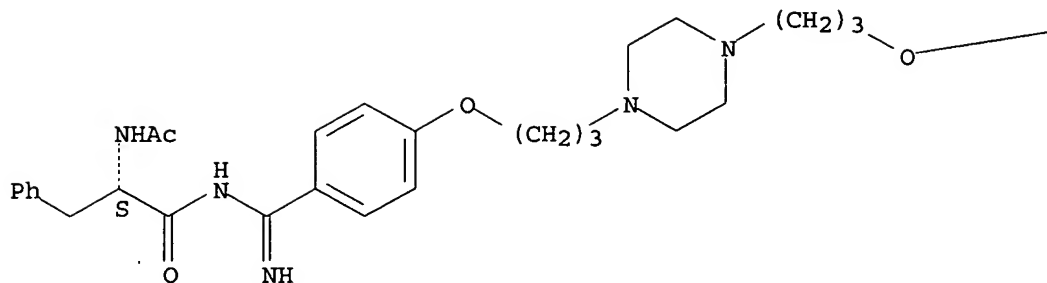
RN 596809-41-5 HCAPLUS

CN Benzenepropanamide, N,N'-[1,4-piperazinediylbis(3,1-propanediyl-oxy-4,1-phenylenecarbonimidoyl)]bis[α-(acetylamino)-, hydrochloride, (αS,α'S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

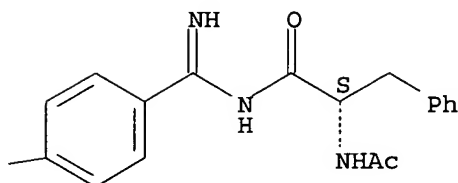


PAGE 1-A



● x HCl

PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:709941 HCAPLUS

DOCUMENT NUMBER: 140:192128

TITLE: Coincubation of tissue slices, a new way to study metabolic cooperation between organs: Hepatorenal cooperation in the biotransformation of CGP 47 969 A

AUTHOR(S): Kretz, O.; Guenat, C.; Beilstein, P.; Gross, G.

CORPORATE SOURCE: PCS-Europe ADME, Novartis Pharma, Basel, CH-4002, Switz.

SOURCE: Journal of Pharmacological and Toxicological Methods (2002), 48(2), 119-126

CODEN: JPTMEZ; ISSN: 1056-8719

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB There is limited information on in vitro/ex vivo tools to be used for studying interorgan metabolic cooperation. We report here the use of the tissue slice technique for this purpose. Rat liver and kidney slices were used to study metabolic cooperation for the metabolism of CGP 47 969, a potential anti-inflammatory compound which in vivo is extensively conjugated with glutathione and subsequently degraded via the mercapturic acid

pathway. Upon incubation with liver slices, CGP 47 969 was extensively conjugated with GSH while degradation of the GSH conjugate was moderate. Upon incubation with kidney slices, conjugation of CGP 47 969 with GSH was moderate but degradation of the GSH conjugate was complete. Upon coincubation of CGP 47 969 with liver and kidney slices, both conjugation with GSH and its subsequent degradation were almost complete. Thus, coincubation of liver and kidney slices permitted the efficient in vitro reproduction of the complete biotransformation of CGP 47 969 via its GSH conjugate to the ultimate mercapturic acid metabolite in a one step procedure. This novel slice coincubation culture could serve as an in vitro model for interorgan cooperation in multistep metabolic processing.

IT 160580-45-0 160580-46-1 160580-47-2

160580-50-7 160580-54-1 663173-96-4

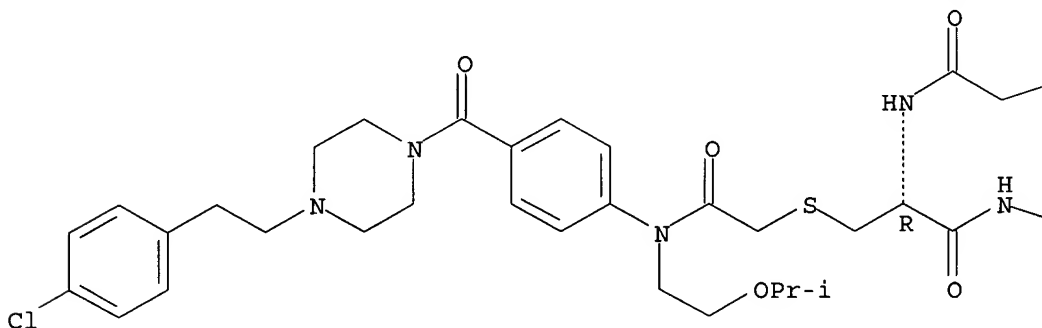
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(coincubation of tissue slices, a new way to study metabolic  
cooperation between organs: hepatorenal cooperation in the  
biotransformation of CGP 47 969 A)

RN 160580-45-0 HCAPLUS

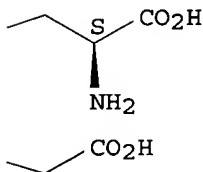
CN Glycine, N-[S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-N-L-γ-glutamyl-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

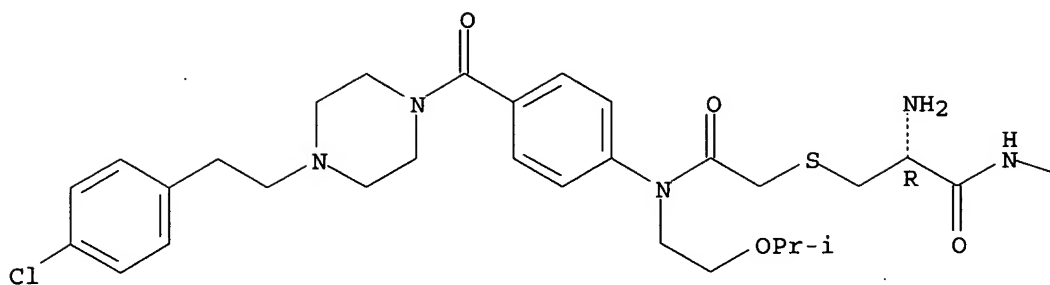


RN 160580-46-1 HCAPLUS

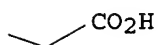
CN Glycine, N-[S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

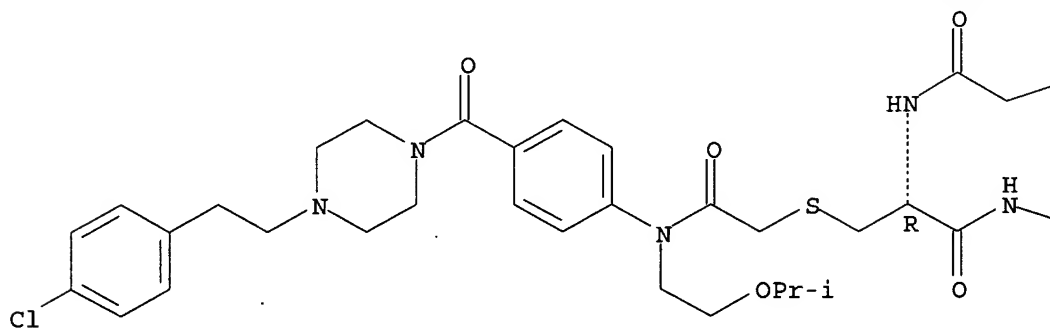


RN 160580-47-2 HCAPLUS

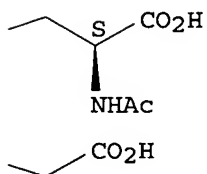
CN Glycine, N-[N-(N-acetyl-L-γ-glutamyl)-S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

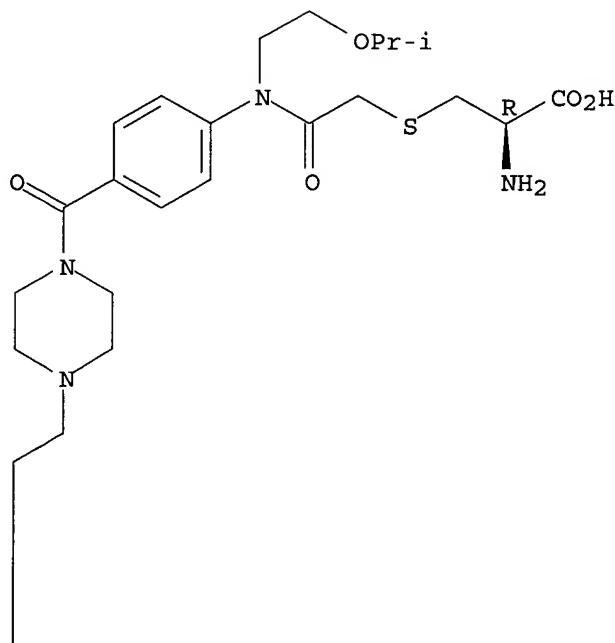


RN 160580-50-7 HCAPLUS

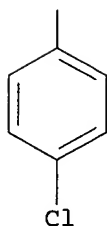
CN L-Cysteine, S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

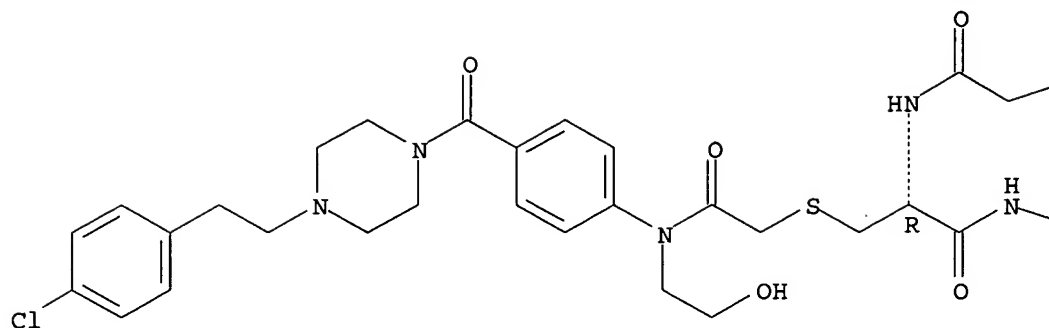


RN 160580-54-1 HCAPLUS

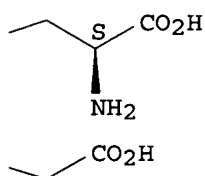
CN Glycine, N-[S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-hydroxyethyl]amino]-2-oxoethyl]-N-L-γ-glutamyl-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



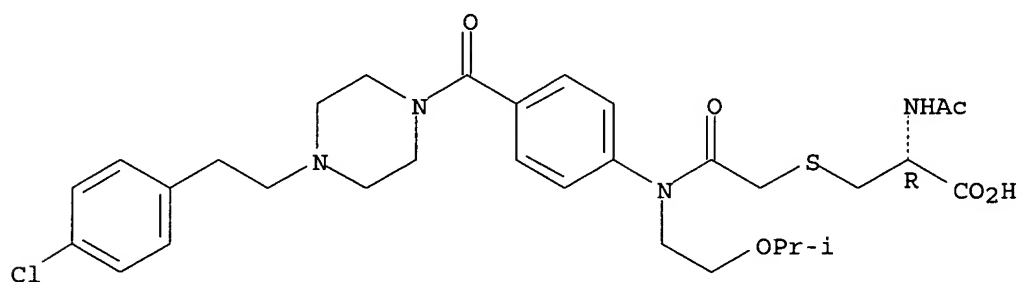
PAGE 1-B



RN 663173-96-4 HCAPLUS

CN L-Cysteine, N-acetyl-S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:335088 HCAPLUS

DOCUMENT NUMBER: 138:354006

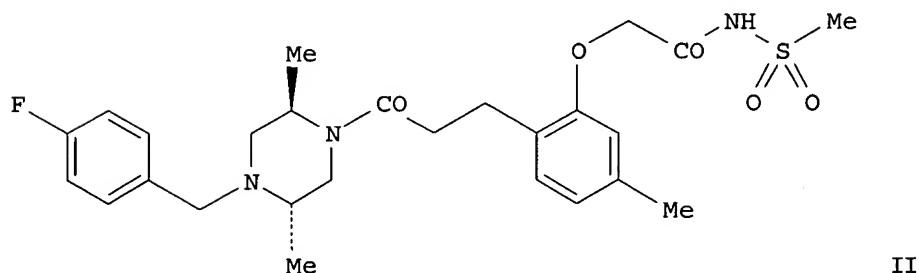
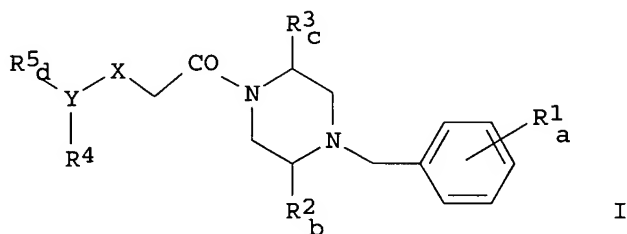
TITLE: Preparation of piperazine derivatives with CCR1 receptor antagonist activity

INVENTOR(S): Blumberg, Laura Cook; Brown, Matthew Frank; Hayward, Matthew Merrill; Poss, Christopher Stanley; Lundquist, Gregory Dean, Jr.; Shavnya, Andrei

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 139 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035627	A1	20030501	WO 2002-IB3989	20020926
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW:				
GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1438298	A1	20040721	EP 2002-772651	20020926
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
EE 200400088	A	20041015	EE 2004-88	20020926
BR 2002013452	A	20041109	BR 2002-13452	20020926
JP 2005507923	T2	20050324	JP 2003-538143	20020926
US 2004034034	A1	20040219	US 2002-273658	20021018
PRIORITY APPLN. INFO.:			US 2001-338601P	P 20011022
			WO 2002-IB3989	W 20020926
OTHER SOURCE(S):		MARPAT 138:354006		
GI				

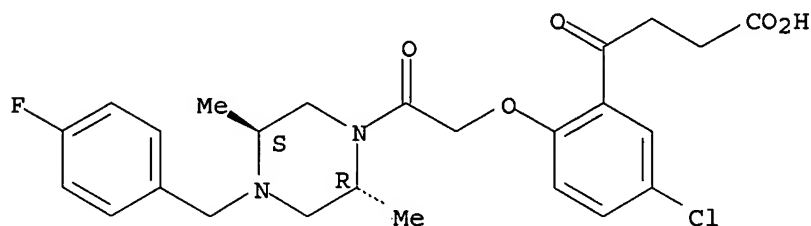


AB The present invention relates to piperazine derivs. (shown as I; variables defined below; e.g. N-[[2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-

dimethylpiperazin-1-yl]-3-oxopropyl]-5-methylphenoxy]acetyl]methanesulfonamide (shown as II)) and the pharmaceutically acceptable forms thereof. Moreover, the present invention is also directed at pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier. Furthermore, the present invention is directed at methods of using the herein described compds. and compns. for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the 15 CCR1 receptor in a mammal. For I: a = 0-5; b = 0-2; c = 0-2; d = 0-4; X = O, S, CH<sub>2</sub>, or NR<sub>6</sub>; Y = (C<sub>6</sub>-C<sub>10</sub>)aryl or (C<sub>2</sub>-C<sub>9</sub>)heteroaryl; each R<sub>1</sub> = H, HO, halo, (C<sub>1</sub>-C<sub>8</sub>)alkyl, (C<sub>1</sub>-C<sub>8</sub>)alkylO, HO(C<sub>1</sub>-C<sub>8</sub>)alkyl, NC, H<sub>2</sub>N, H<sub>2</sub>N(C<sub>1</sub>-C<sub>8</sub>)alkyl, HO<sub>2</sub>C, (C<sub>1</sub>-C<sub>8</sub>)alkylC(O), (C<sub>1</sub>-C<sub>8</sub>)alkylC(O)(C<sub>1</sub>-C<sub>8</sub>)alkyl, H<sub>2</sub>NC(O), or H<sub>2</sub>NC(O)(C<sub>1</sub>-C<sub>8</sub>)alkyl. Each R<sub>2</sub> and R<sub>3</sub> = H, oxo, (C<sub>1</sub>-C<sub>8</sub>)alkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl(C<sub>1</sub>-C<sub>8</sub>)alkyl, (C<sub>6</sub>-C<sub>10</sub>)aryl, etc. R<sub>4</sub> = (HO<sub>2</sub>C)(H<sub>2</sub>N)(C<sub>1</sub>-C<sub>8</sub>)alkyl, (HO<sub>2</sub>C)[[(C<sub>1</sub>-C<sub>8</sub>)alkyl]NH](C<sub>1</sub>-C<sub>8</sub>)alkyl, (HO<sub>2</sub>C)[[(C<sub>1</sub>-C<sub>8</sub>)alkyl]2N](C<sub>1</sub>-C<sub>8</sub>)alkyl, etc.; R<sub>5</sub> = H, HO, halo, NC, HO<sub>2</sub>C, H<sub>2</sub>N, (C<sub>1</sub>-C<sub>8</sub>)alkylNH, [(C<sub>1</sub>-C<sub>8</sub>)alkyl]2N, etc.; R<sub>6</sub> = H, (C<sub>1</sub>-C<sub>8</sub>)alkyl, (C<sub>1</sub>-C<sub>8</sub>)alkylC(O), (C<sub>6</sub>-C<sub>10</sub>)arylC(O), (C<sub>2</sub>-C<sub>9</sub>)heteroarylC(O), H<sub>2</sub>NC(O), (C<sub>1</sub>-C<sub>8</sub>)alkylNHC(O), [(C<sub>1</sub>-C<sub>8</sub>)alkyl]2NC(O), (C<sub>1</sub>-C<sub>8</sub>)alkylOC(O), or (C<sub>1</sub>-C<sub>8</sub>)alkylSO<sub>2</sub>; addnl. details are given in the claims. Although the methods of preparation are not claimed, 47 example preps. and characterization data (mass spectral parent ion mass) for 259 examples of I are included. I are potent and selective inhibitors of MIP-1 $\alpha$  (CCL3) binding to its receptor CCR1 found on inflammatory and immunomodulatory cells (preferably leukocytes and lymphocytes). These compds. also inhibit MIP-1 $\alpha$  (and the related chemokines shown to interact with CCR1)-induced chemotaxis of THP-1 cells and human leukocytes. All I in the examples had IC<sub>50</sub> of <10  $\mu$ M in the MIP-1 $\alpha$ -induced chemotaxis assay.

IT **519171-87-0P**, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-oxobutyric acid  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (drug candidate; preparation of piperazine derivs. with CCR1 receptor antagonist activity)  
 RN 519171-87-0 HCAPLUS  
 CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]- $\gamma$ -oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **519171-89-2P**, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid hydrochloride **519172-90-8P**, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-oxopentanoic acid **519173-17-2P**, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]oxoacetic acid **519173-72-9P**, [3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-

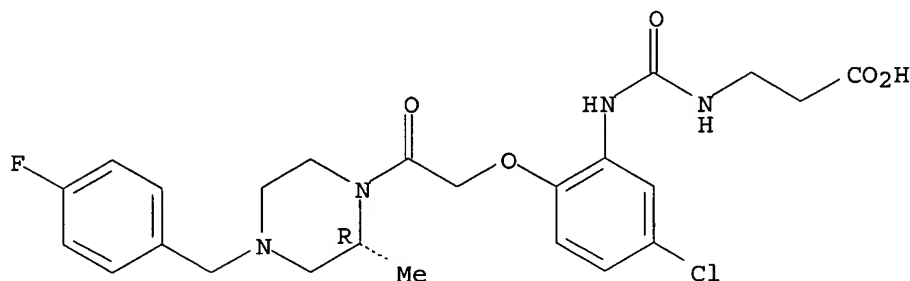
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]acetic acid  
**519173-73-0P**, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid  
**519173-74-1P**, 3-[3-[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid  
**519173-75-2P**, [3-[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]acetic acid  
**519174-44-8P**, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]amino]oxoacetic acid  
**519174-74-4P**, [[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonyl]amino]oxoacetic acid  
**519174-76-6P**, [[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonyl]amino]oxoacetic acid  
**519175-34-9P**, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid  
**519175-35-0P**, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-oxobutyric acid  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperazine derivs. with CCR1 receptor antagonist activity)

RN 519171-89-2 HCAPLUS

CN  $\beta$ -Alanine, N-[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



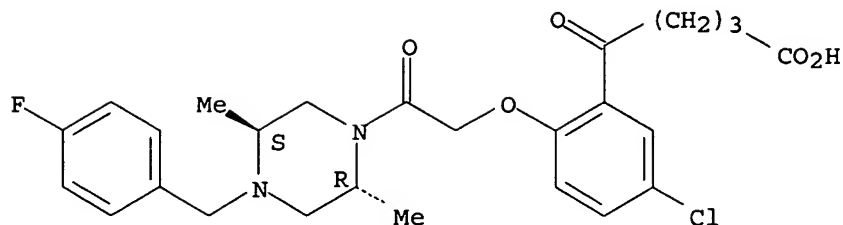
●x HCl

RN 519172-90-8 HCAPLUS

CN Benzenepentanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-8-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

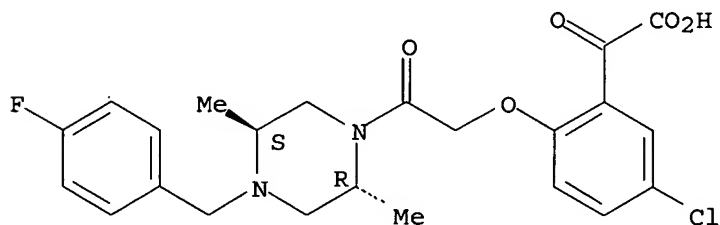




RN 519173-17-2 HCAPLUS

CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-α-oxo- (9CI) (CA INDEX NAME)

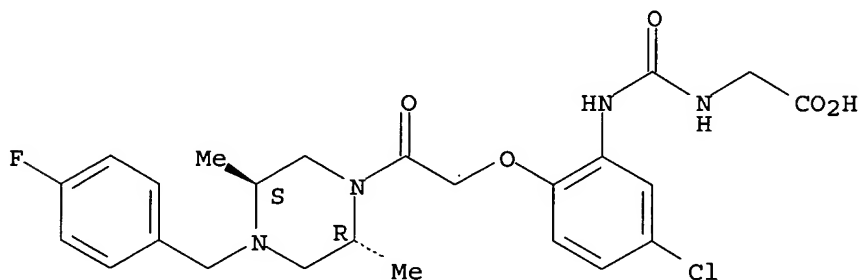
Absolute stereochemistry.



RN 519173-72-9 HCAPLUS

CN Glycine, N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

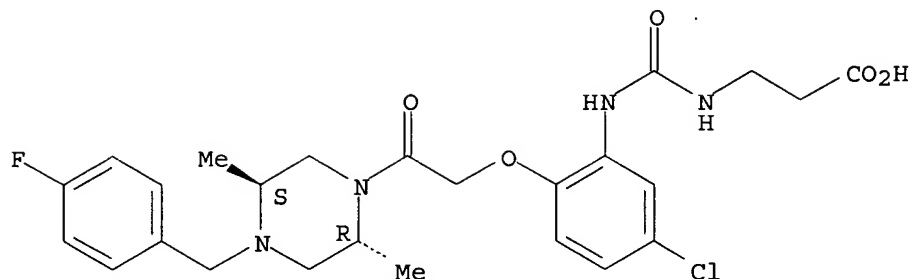
Absolute stereochemistry.



RN 519173-73-0 HCAPLUS

CN β-Alanine, N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

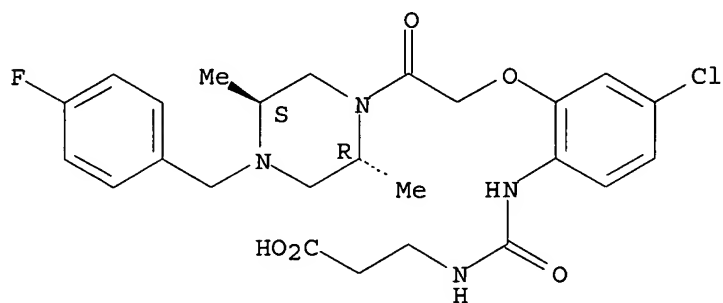
Absolute stereochemistry.



RN 519173-74-1 HCAPLUS

CN  $\beta$ -Alanine, N-[[[4-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

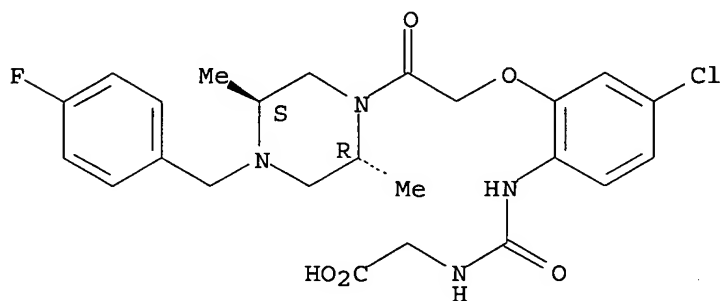
Absolute stereochemistry.



RN 519173-75-2 HCAPLUS

CN Glycine, N-[[[4-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

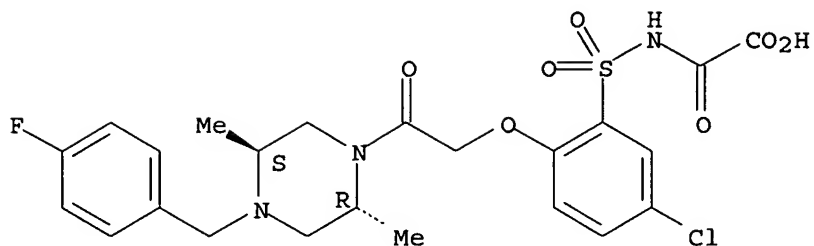
Absolute stereochemistry.



RN 519174-44-8 HCAPLUS

CN Acetic acid, [[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

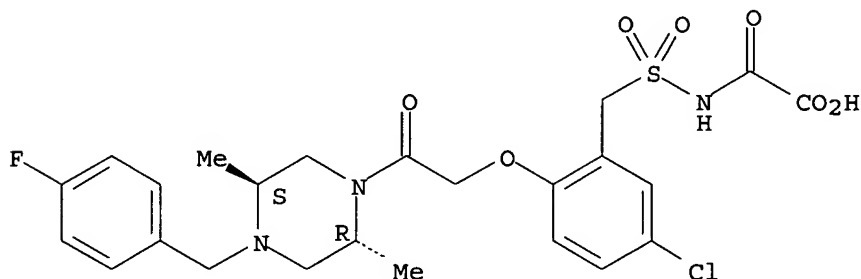
Absolute stereochemistry.



RN 519174-74-4 HCAPLUS

CN Acetic acid, [[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

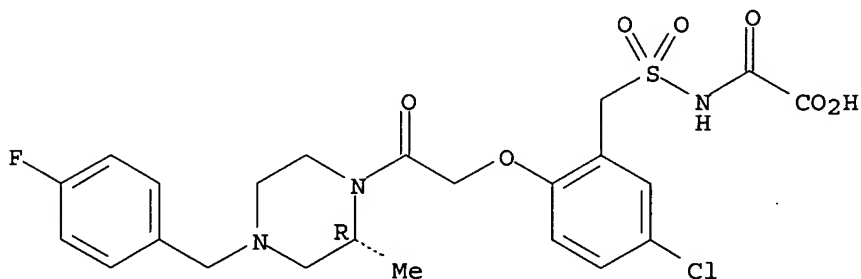
Absolute stereochemistry.



RN 519174-76-6 HCAPLUS

CN Acetic acid, [[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]sulfonyl]amino]oxo- (9CI) (CA INDEX NAME)

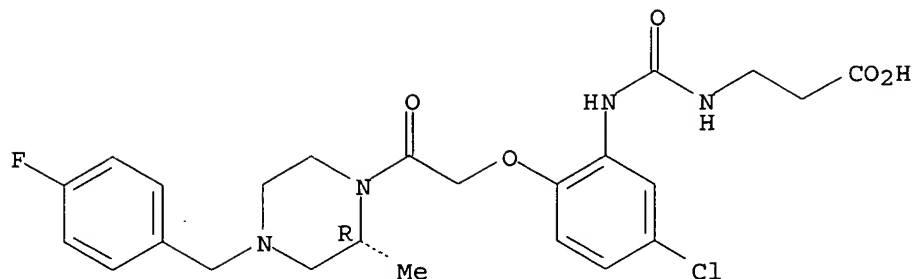
Absolute stereochemistry.



RN 519175-34-9 HCAPLUS

CN beta-Alanine, N-[[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

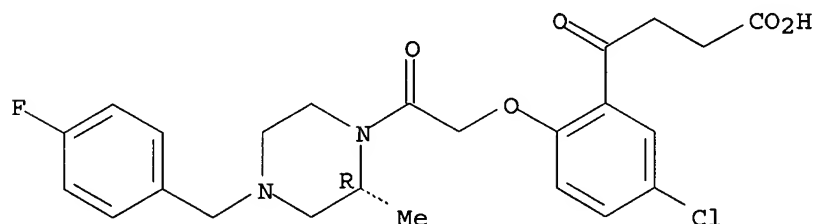
Absolute stereochemistry.



RN 519175-35-0 HCAPLUS

CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]-gamma-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

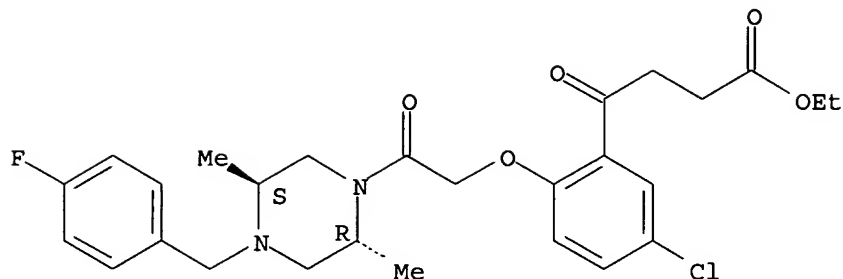


IT 519171-88-1P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-4-oxobutyric acid ethyl ester  
 519171-91-6P, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid methyl ester  
 519172-23-7P, Acetic acid 2-[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]amino]-1,1-dimethyl-2-oxoethyl ester.  
 519172-31-7P, Acetic acid 2-[[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonyl]amino]-1,1-dimethyl-2-oxoethyl ester  
 519172-93-1P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-oxopentanoic acid ethyl ester  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of piperazine derivs. with CCR1 receptor antagonist activity)

RN 519171-88-1 HCAPLUS

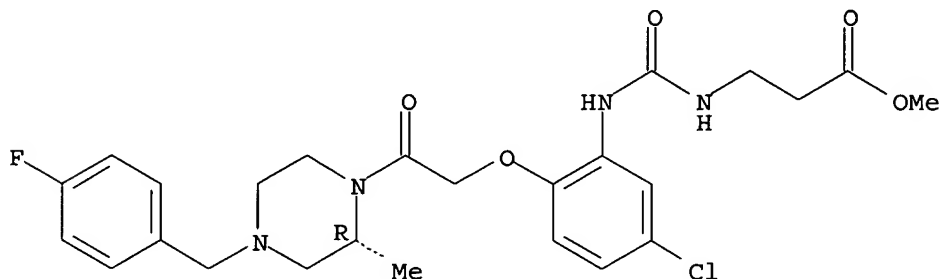
CN Benzenebutanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-gamma-oxo-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



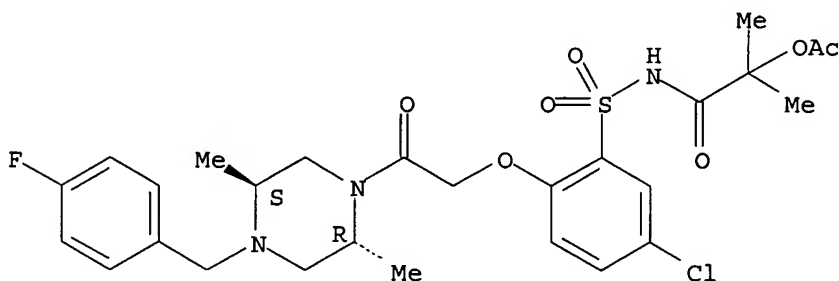
RN 519171-91-6 HCAPLUS  
 CN  $\beta$ -Alanine, N-[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperaziny]-2-oxoethoxy]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



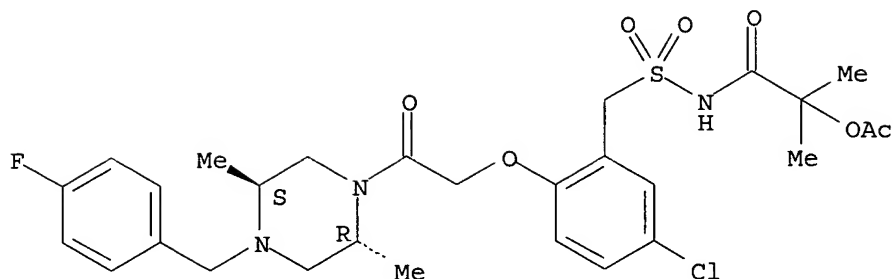
RN 519172-23-7 HCAPLUS  
 CN Propanamide, 2-(acetyloxy)-N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperaziny]-2-oxoethoxy]phenyl]sulfonyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 519172-31-7 HCAPLUS  
 CN Propanamide, 2-(acetyloxy)-N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperaziny]-2-oxoethoxy]phenyl]methyl]sulfonyl]-2-methyl- (9CI) (CA INDEX NAME)

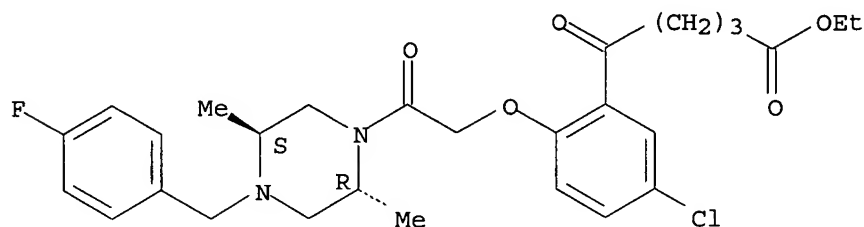
Absolute stereochemistry.



RN 519172-93-1 HCAPLUS

CN Benzenepentanoic acid, 5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-8-oxo-, ethyl ester (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:62666 HCAPLUS

DOCUMENT NUMBER: 138:89825

TITLE: Preparation of thiazolyl-benzyl-piperazines for treating gastrointestinal disorders

INVENTOR(S): Maw, Graham Nigel

PATENT ASSIGNEE(S): Pfizer Limited, UK

SOURCE: Brit. UK Pat. Appl., 52 pp.

CODEN: BAXXDU

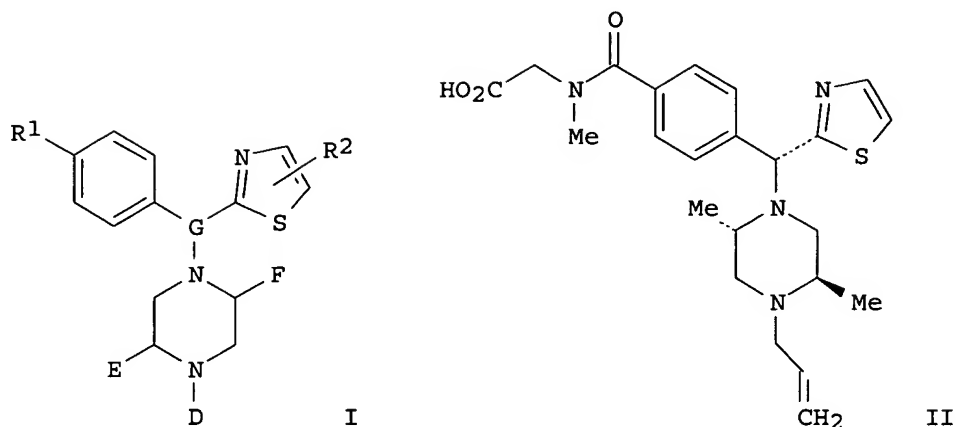
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2374074	A1	20021009	GB 2002-3197	20020211
PRIORITY APPLN. INFO.:			GB 2001-5098	A 20010301
OTHER SOURCE(S):	MARPAT	138:89825		
GI				



AB Thiazolyl-benzyl-piperazines [I; wherein G = C(H), C((C1-C4)alkyl); D = H, (C1-C10)alkyl, aryl; E, F, independently = H, Me; R1 = CO-R3 (wherein R3 is the residue of an optionally N-alkyl or -aryl substituted amino acid or a biolabile ester), tetrazolyl; R2 = H, (C1-C10)alkyl, aryl] were prepared. For example, 2-[[4-[[R]-[[2S,5R]-4-allyl-2,5-dimethylpiperazinyl]-[1,3-thiazol-2-yl]methyl]benzoyl][methyl]amino]acetic acid (II) was prepared in several steps. The prepared compds. are agonists for the  $\delta$ -opioid receptor and, thus, are useful in the treatment of gastrointestinal disorders. For example, compound II showed MVD pIC<sub>50</sub> = 8.90 against the  $\delta$ -opioid receptor.

IT 482604-53-5P 482604-54-6P

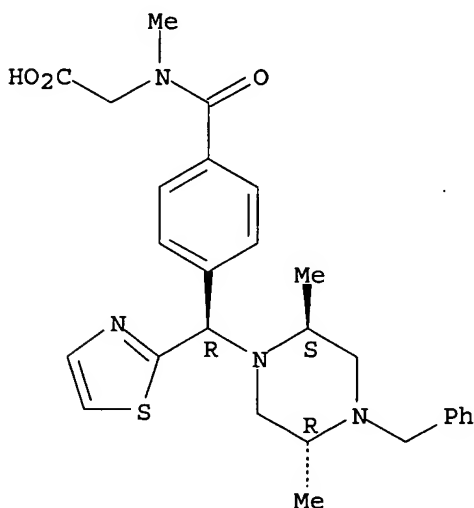
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of thiazolyl-benzyl-piperazines for treating gastrointestinal disorders)

RN 482604-53-5 HCAPLUS

CN Glycine, N-[4-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl]-2-thiazolylmethyl]benzoyl]-N-methyl- (9CI) (CA INDEX NAME)

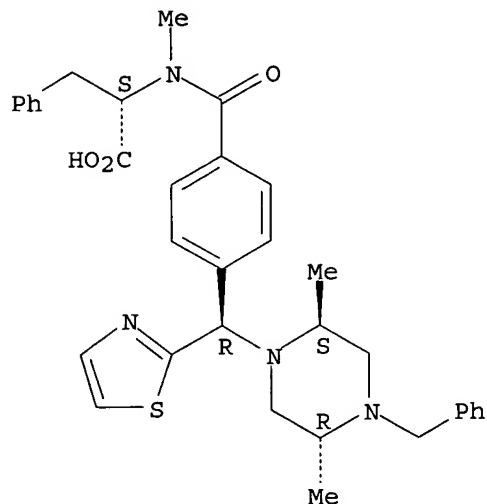
Absolute stereochemistry.



RN 482604-54-6 HCAPLUS

CN L-Phenylalanine, N-[4-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl]-2-thiazolylmethyl]benzoyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



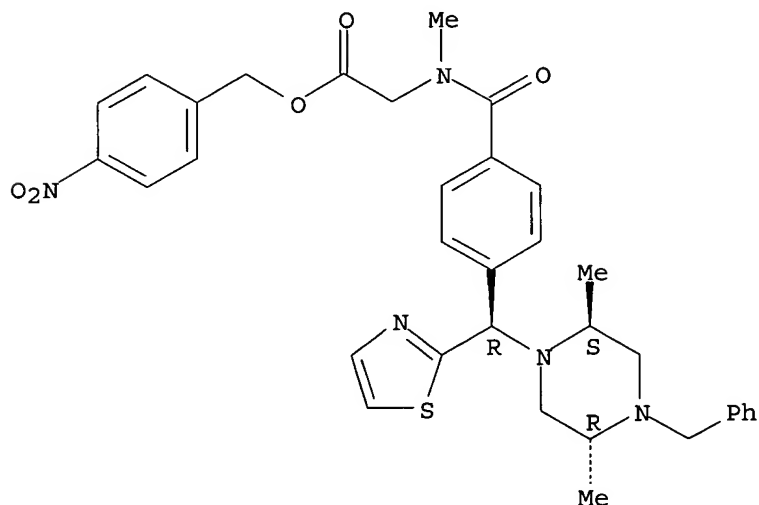
IT 482604-70-6P 482604-71-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of thiazolyl-benzyl-piperazines for treating gastrointestinal disorders)

RN 482604-70-6 HCAPLUS

CN Glycine, N-[4-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl]-2-thiazolylmethyl]benzoyl]-N-methyl-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

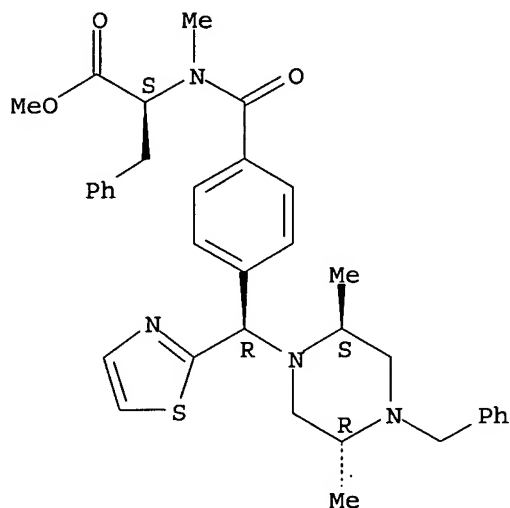


RN 482604-71-7 HCAPLUS



CN L-Phenylalanine, N-[4-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl]-2-thiazolylmethyl]benzoyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 10 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:964345 HCAPLUS

DOCUMENT NUMBER: 138:24952

TITLE: Preparation of novel amino nitriles useful as reversible inhibitors of cysteine proteases  
INVENTOR(S): Hickey, Eugene R.; Bekkali, Younes; Patel, Usha R.; Spero, Denice M.; Thomson, David S.; Young, Erick R.

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 223 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100849	A2	20021219	WO 2002-US17590	20020605
WO 2002100849	A3	20031016		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003119827	A1	20030626	US 2002-163015	20020604
CA 2449192	AA	20021219	CA 2002-2449192	20020605

EP 1399431 A2 20040324 EP 2002-741825 20020605  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2005501017 T2 20050113 JP 2003-503617 20020605  
 PRIORITY APPLN. INFO.: US 2001-296863P P 20010608  
 WO 2002-US17590 W 20020605

OTHER SOURCE(S): MARPAT 138:24952

AB Novel nitrile compds. YCO<sub>2</sub>CR<sub>2</sub>R<sub>3</sub>C(:X)NR<sub>6</sub>CR<sub>4</sub>R<sub>5</sub>CN [Y = R<sub>1</sub>, R<sub>10</sub>, R<sub>1S</sub>, R<sub>12N</sub>, R<sub>13C</sub>, where R<sub>1</sub> = H, (un)substituted (cyclo)alkyl, aryl, benzyl, tetrahydronaphthyl, indenyl, indanyl, alkylsulfonylalkyl, cycloalkylsulfonylalkyl, arylsulfonylalkyl, heterocyclyl, or heteroaryl; R<sub>2</sub>-R<sub>5</sub> = H, (un)substituted (cyclo)alkyl, aryl, etc. or CR<sub>2</sub>R<sub>3</sub> and CR<sub>4</sub>R<sub>5</sub> may form rings; R<sub>6</sub> = H, OH, or (cyclo)alkyl; X = O or S (with provisos)] or their pharmaceutically-acceptable derivs. were prepared as reversible inhibitors of cysteine proteases such as cathepsin K, S, F, L and B for treating diseases and pathol. conditions exacerbated by these proteases such as osteoporosis, rheumatoid arthritis, multiple sclerosis, asthma and other autoimmune diseases, Alzheimer's disease, and atherosclerosis. Thus, morpholine-4-carboxylic acid 1-[[[benzyloxymethyl]cyanomethyl]carbamoyl]-3-methylbutyl ester was prepared from N-(tert-butoxycarbonyl)-O-benzyl-L-serine, 2-Hydroxyisocaproic acid, and 4-morpholinecarbonyl chloride.

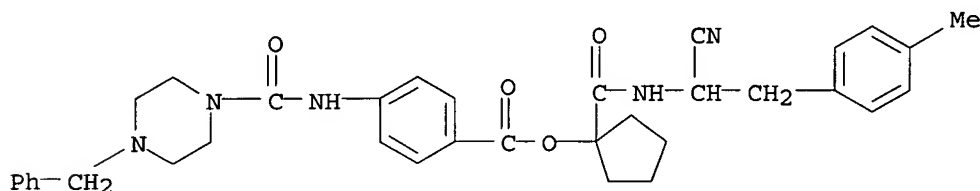
IT 478280-25-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of novel amino nitriles as reversible inhibitors of cysteine proteases)

RN 478280-25-0 HCAPLUS

CN Benzoic acid, 4-[[[4-(phenylmethyl)-1-piperazinyl]carbonyl]amino]-, 1-[[[1-cyano-2-(4-methylphenyl)ethyl]amino]carbonyl]cyclopentyl ester (9CI) (CA INDEX NAME)



L12 ANSWER 11 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:353444 HCAPLUS

DOCUMENT NUMBER: 136:379069

TITLE: Radiopharmaceuticals for diagnosing Alzheimer's disease

INVENTOR(S): Hilger, Christoph-Stephan; Johannsen, Bernd; Steinbach, Joerg; Maeding, Peter; Halks-Miller, Meredith; Horuk, Richard; Dinter, Harald; Mohan, Raju; Hesselgesser, Joseph E.

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

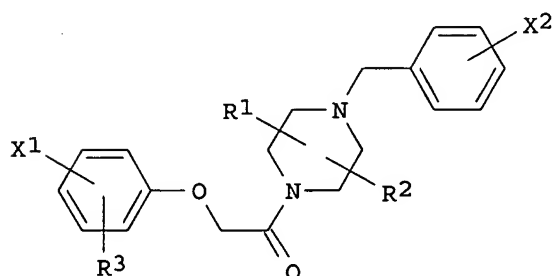
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036581	A1	20020510	WO 2001-EP12607	20011101
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2424598	AA	20020510	CA 2001-2424598	20011101
AU 2002014034	A5	20020515	AU 2002-14034	20011101
EP 1332138	A1	20030806	EP 2001-982450	20011101
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300216	A	20030815	EE 2003-216	20011101
BR 2001015150	A	20031230	BR 2001-15150	20011101
JP 2004513123	T2	20040430	JP 2002-539340	20011101
NZ 525303	A	20041029	NZ 2001-525303	20011101
US 2002131932	A1	20020919	US 2001-985938	20011106
US 6676926	B2	20040113		
BG 107762	A	20040331	BG 2003-107762	20030425
NO 2003002007	A	20030702	NO 2003-2007	20030505
ZA 2003004409	A	20040906	ZA 2003-4409	20030605
US 6872381	B1	20050329	US 2003-626725	20030725
PRIORITY APPLN. INFO.:			US 2000-246299P	P 20001106
			WO 2001-EP12607	W 20011101
			US 2001-985938	A1 20011106
OTHER SOURCE(S):			MARPAT 136:379069	
GI				



I

- AB I (X1 and X2 are independently halo; R1 and R2 are independently H or alkyl; R3 = H, amino, alkylamino, aralkylamino, alkylcarbonylamino, alkenylcarbonylamino, glycinamido, ureido, etc.) were prepared and complexed with <sup>99m</sup>Tc to form complexes that are useful as imaging agents in the early diagnosing Alzheimer's disease. In particular the radiopharmaceuticals of the invention are able to pass through the blood-brain barrier and bind to the CCR1 receptor present in brain tissue of patients having Alzheimer's disease.
- IT 422270-36-8P 422270-44-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and complexation with technetium)

RN 422270-36-8 HCAPLUS  
 CN Glycinamide, N-(2-mercaptoethyl)-N-[2-[(2-mercaptoethyl)amino]-2-oxoethyl]glycyl-N-[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]-, bis(trifluoroacetate) (salt) (9CI)  
 (CA INDEX NAME)

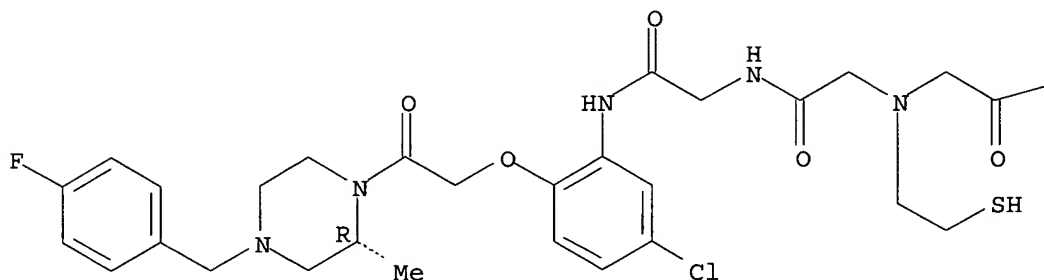
CM 1

CRN 422270-35-7

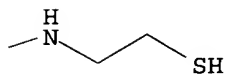
CMF C30 H40 Cl F N6 O5 S2

Absolute stereochemistry.

PAGE 1-A



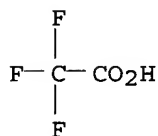
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 422270-44-8 HCAPLUS  
 CN Acetamide, 2-[[2-[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl](2-mercaptoethyl)amino]-N-(2-mercaptoethyl)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

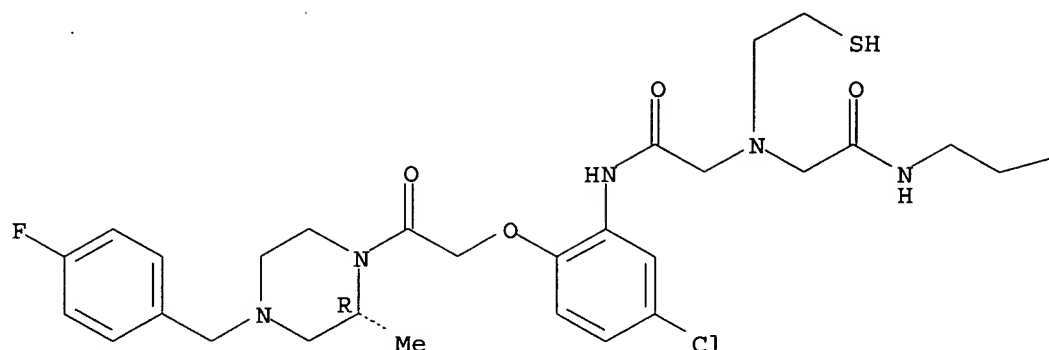
CM 1

CRN 422270-23-3

CMF C28 H37 Cl F N5 O4 S2

Absolute stereochemistry.

PAGE 1-A



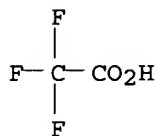
PAGE 1-B

—SH

CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 422270-33-5P 422270-34-6P 422270-43-7P

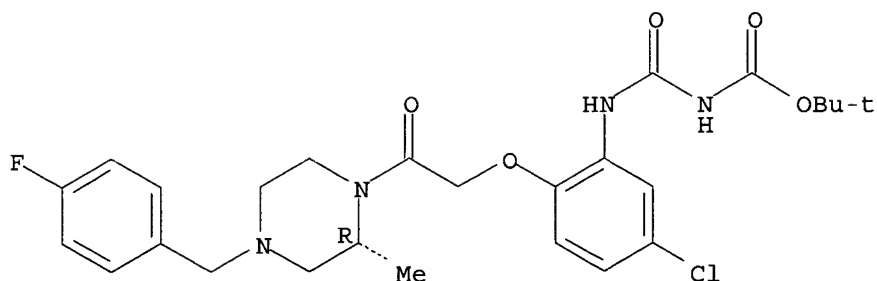
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reactant for preparation of technetium piperazinyloxyethoxyphenylurea and -glycinamide complexes as imaging agents for diagnosing Alzheimer's disease)

RN 422270-33-5 HCAPLUS

CN Carbamic acid, [[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

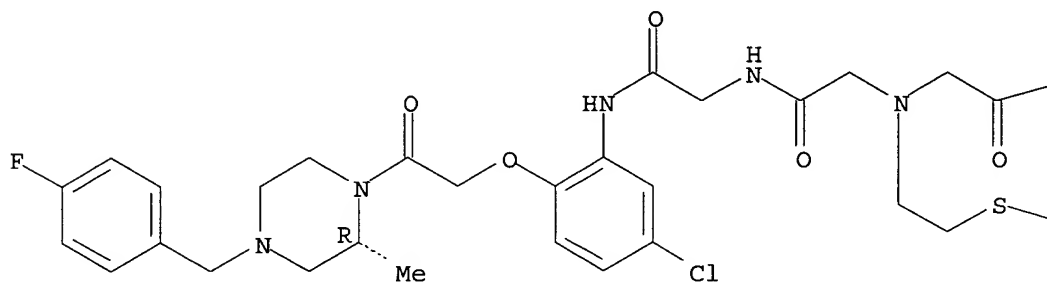


RN 422270-34-6 HCAPLUS

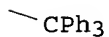
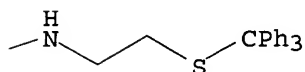
CN Glycinamide, N-[2-oxo-2-[[2-[(triphenylmethyl)thio]ethyl]amino]ethyl]-N-[2-[[2-[(triphenylmethyl)thio]ethyl]glycyl-N-5-chloro-2-[[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

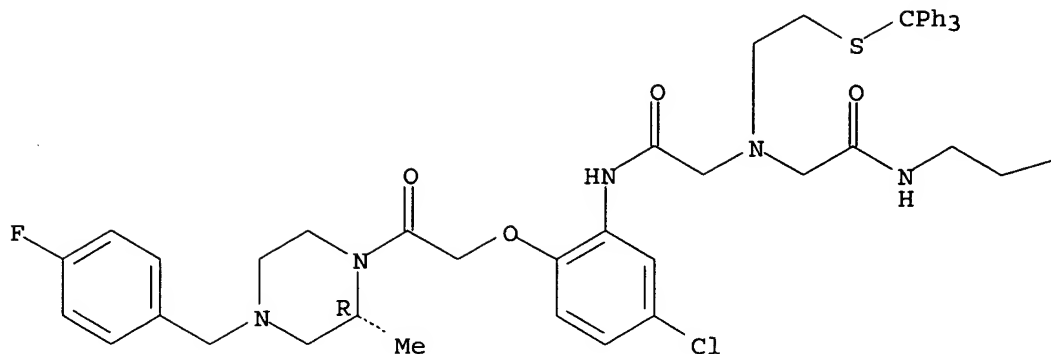


RN 422270-43-7 HCAPLUS

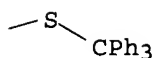
CN Acetamide, 2-[[2-[[5-chloro-2-[[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl][2-[[2-[(triphenylmethyl)thio]ethyl]amino]-N-[2-[(triphenylmethyl)thio]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



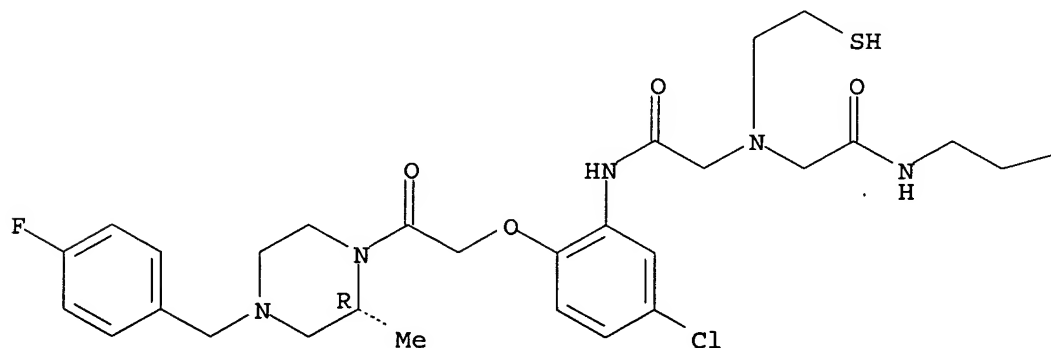
PAGE 1-B



IT 422270-23-3DP, technetium-99m complex 422270-35-7DP,  
 technetium-99m complex  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (preparation as imaging agent for diagnosing Alzheimer's disease)  
 RN 422270-23-3 HCAPLUS  
 CN Acetamide, 2-[[2-[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-  
 1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl](2-  
 mercaptoethyl)amino]-N-(2-mercaptoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



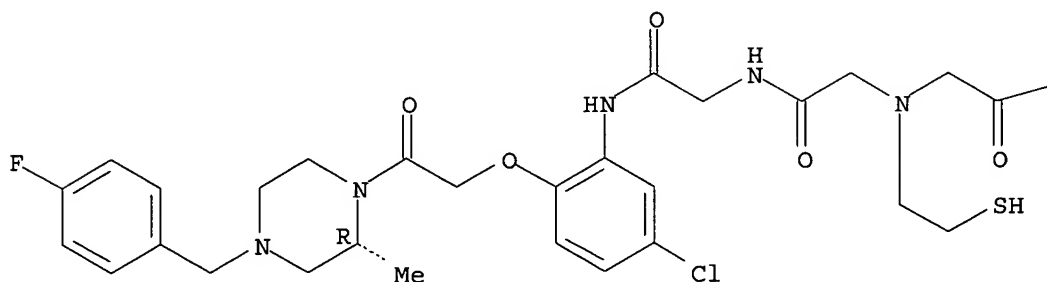
PAGE 1-B

—SH

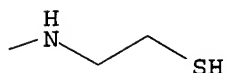
RN 422270-35-7 HCAPLUS  
 CN Glycinamide, N-(2-mercaptoethyl)-N-[2-[(2-mercaptoethyl)amino]-2-oxoethyl]glycyl-N-[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:221217 HCAPLUS  
 DOCUMENT NUMBER: 136:247349  
 TITLE: Preparation of amino(oxo)acetic acid derivatives as protein tyrosine phosphatase inhibitors  
 INVENTOR(S): Liu, Gang; Li, Yihong; Janowick, David A.; Pei, Zhonghua  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 28 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002035136	A1	20020321	US 2001-934765	20010822
US 6627767	B2	20030930		



PRIORITY APPLN. INFO.:

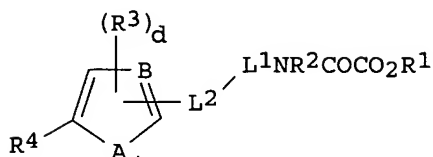
US 2000-228656P

P 20000829

OTHER SOURCE(S):

MARPAT 136:247349

GI



I

AB The title compds. I [A = NH, O, S, N:CH, CH:CH; B = N, CH; d = 0-2; L1 = bond, O; L2 = CHR6, CH2CHR6; R1 = H, carboxy protecting group; R2 = H, aminoalkyl, alkyl, cycloalkyl, etc.; R3 = H, alkoxy, alkoxyalkenyl, carboxy, etc.; R4 = H, alkoxy, aryl, heteroaryl, etc.], protein tyrosine kinase PTP1B inhibitors, were prepared. E.g., N-benzyl-2-hydroxy-N-((4,1'-binaphth-1-yl)methyl)amino(oxo)acetic acid was prepared I may be used for treatment of type II diabetes or obesity.

IT 402935-87-9P

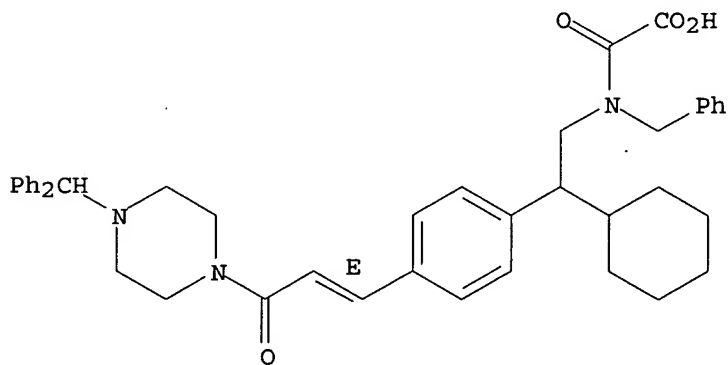
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino(oxo)acetic acid derivs. as protein tyrosine phosphatase inhibitors)

RN 402935-87-9 HCAPLUS

CN Acetic acid, [[2-cyclohexyl-2-[4-[(1E)-3-[4-(diphenylmethyl)-1-piperazinyl]-3-oxo-1-propenyl]phenyl]ethyl](phenylmethyl)amino]oxo- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



L12 ANSWER 13 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:171839 HCAPLUS

DOCUMENT NUMBER: 136:232060

TITLE: Preparation of amino(oxo)acetic acid protein tyrosine phosphatase inhibitors

INVENTOR(S): Liu, Gang; Li, Yihong; Janowick, David A.; Pei, Zhonghua

PATENT ASSIGNEE(S): Abbott Laboratories, USA

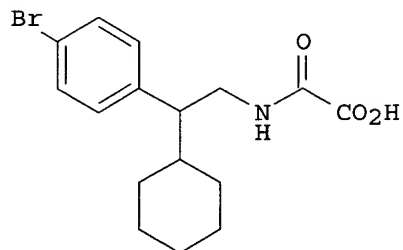
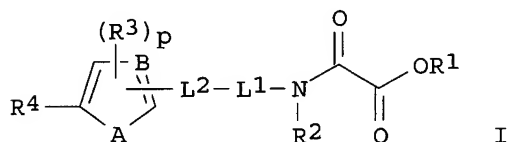
SOURCE: PCT Int. Appl., 61 pp.

DOCUMENT TYPE: CODEN: PIXXD2  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: 1 English  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018321	A2	20020307	WO 2001-US26133	20010821
WO 2002018321	A3	20030410		

W: CA, JP, MX  
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-650923 A 20000829  
 OTHER SOURCE(S): MARPAT 136:232060  
 GI

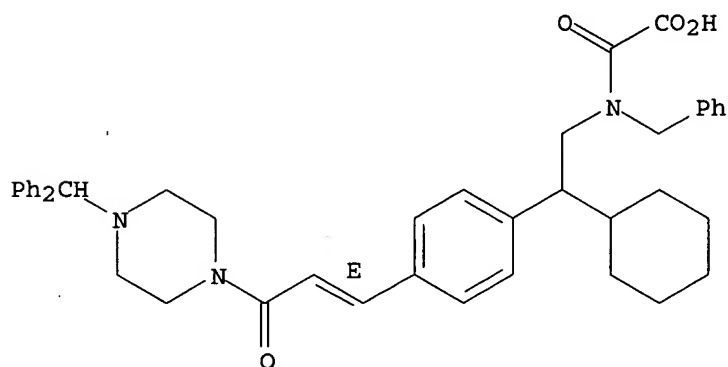


AB Title compds. I [A = N(H), O, S, N=C(H), C(H)=C(H), etc.; B = N, C(H); with the proviso that when A is N=C(H) or C(H)=C(H), B is C(H); p = 0-2; L<sub>1</sub> = bond, O; L<sub>2</sub> = CHR<sub>6</sub>, CH<sub>2</sub>CHR<sub>6</sub>; R<sub>1</sub> = H, carboxy protecting group; R<sub>2</sub> = H, aminoalkyl, cycloalkyl(alkyl), cycloalkenyl(alkyl), (hetero)aryl, heterocycle, etc.; R<sub>3</sub> = H, alkoxy, alkoxyalk(en)yl, alkoxyalkoxy, alkoxyacarbonyl, alkoxyacarbonylalkyl, alkoxyacarbonylalkenyl, alkoxyacarbonylalkoxy, aryl, arylalkyl, arylalkenyl, arylalkoxy, carboxamido, carboxamidoalkyl, etc.; R<sub>4</sub> = H, alkoxy, loweralkoxy, alkoxyacarbonylalkyl, alkoxyacarbonylalkenyl, aryl, arylalkyl, arylalkoxy, arylthioxyalkyl, carboxamidoalkenyl, carboxamidoalkyl, carboxyalkyl, carboxyalkenyl, heteroaryl, etc.; with the proviso that at when R<sub>4</sub> = H, at least one of R<sub>3</sub> is other than H; R<sub>6</sub> = H, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, etc.] were prepared Over 70 synthetic examples were provided. For instance, 4-bromophenylacetonitrile was alkylated with cyclohexyl bromide (DMF/benzene, NaH, 0°C) to give (4-bromophenyl)(cyclohexyl)acetonitrile which was subsequently reduced to the amine (PhMe, DIBAL-H → BH<sub>3</sub>•THF), the amine acylated with Et

oxalyl chloride (CH<sub>2</sub>Cl<sub>2</sub>, 0°C) and saponified to give II. Example compds. were found to inhibit protein tyrosine phosphatase PTP1B with inhibitory potencies in a range of about 3 μM to about 100 μM. I are used for the treatment of type II diabetes and obesity.

IT 402935-87-9P, [[2-[4-[(1E)-3-(4-Benzhydryl-1-piperazinyl)-3-oxo-1-propenyl]phenyl]-2-cyclohexylethyl](benzyl)amino](oxo)acetic acid  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (drug; preparation of amino(oxo)acetic acid protein tyrosine phosphatase inhibitors)  
 RN 402935-87-9 HCAPLUS  
 CN Acetic acid, [[2-cyclohexyl-2-[4-[(1E)-3-[4-(diphenylmethyl)-1-piperazinyl]-3-oxo-1-propenyl]phenyl]ethyl](phenylmethyl)amino]oxo- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.



L12 ANSWER 14 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2001:730721 HCAPLUS  
 DOCUMENT NUMBER: 135:272991  
 TITLE: Preparation of piperazines for use as pharmaceuticals for the treatment of inflammation and other immune disorders  
 INVENTOR(S): Blumberg, Laura Cook; Brown, Matthew Frank; McGlynn, Molly Ann; Poss, Christopher Stanley; Gladue, Ronald Paul  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: PCT Int. Appl., 80 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072728	A2	20011004	WO 2001-IB375	20010314
WO 2001072728	A3	20020718		
WO 2001072728	C2	20021010		
WO 2001072728	B1	20030109		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,  
 RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,  
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

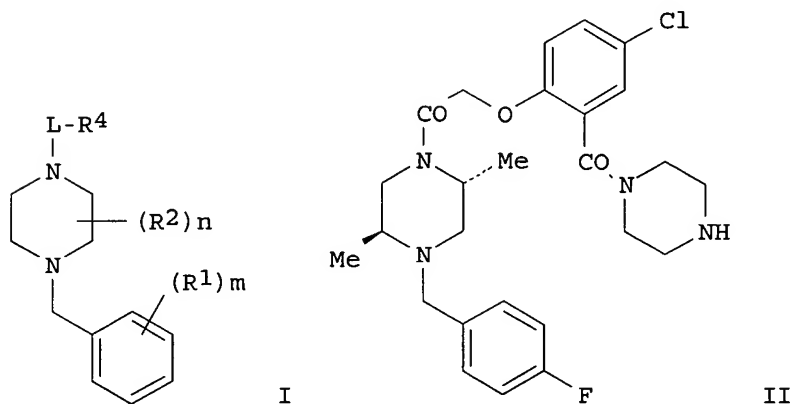
CA 2404626	AA	20011004	CA 2001-2404626	20010314
EP 1268455	A2	20030102	EP 2001-914083	20010314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009703	A	20030204	BR 2001-9703	20010314
JP 2003528867	T2	20030930	JP 2001-570640	20010314
EE 200200567	A	20040615	EE 2002-567	20010314
NZ 521290	A	20041029	NZ 2001-521290	20010314
US 2002107255	A1	20020808	US 2001-821322	20010329
US 6649611	B2	20031118		
BG 107091	A	20030430	BG 2002-107091	20020912
NO 2002004649	A	20020927	NO 2002-4649	20020927
ZA 2002007827	A	20030930	ZA 2002-7827	20020930
US 2004058932	A1	20040325	US 2003-660052	20030910

PRIORITY APPLN. INFO.:

US 2000-193789P	P	20000331
WO 2001-IB375	W	20010314
US 2001-821322	A3	20010329

OTHER SOURCE(S):  
 GI

CASREACT 135:272991; MARPAT 135:272991



AB Piperazines, such as I [R1 = H, OH, SO<sub>3</sub>H, SH, halogen, alkyl, alkylthio, alkoxy, etc.; R2 = oxo, CHO, halogen, alkyl, alkenyl, alkynyl, carboxy, aryl, heteroaryl, etc.; R4 = aryl, cycloalkyl, heteroaryl, heterocyclyl; L = linking group of the form -Xc-Yd-Ze-; X = CO, CS, CH<sub>2</sub>; Y = CH<sub>2</sub>; Z = O, NR<sub>9</sub>, etc.; R<sub>9</sub> = H, alkyl, aryl, etc.; d = 1-5; c, e = 0, 1; m = 1-5; n = 1-4], were prepared for use as pharmaceutical agents for the treatment of inflammation and other immune disorders. Thus, piperazine II was prepared via cyclocondensation of (R)-Me<sub>3</sub>COCONHCH(Me)CO<sub>2</sub>H with (S)-F-4-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>NHCH(Me)CO<sub>2</sub>Me in THF using 4-methylmorpholine and isobutylchloroformate. The prepared piperazines were assayed for their ability to inhibit the chemotaxis to various chemokines. Also, pharmaceutical compns. for delivery of the piperazines were discussed.

IT 364066-85-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

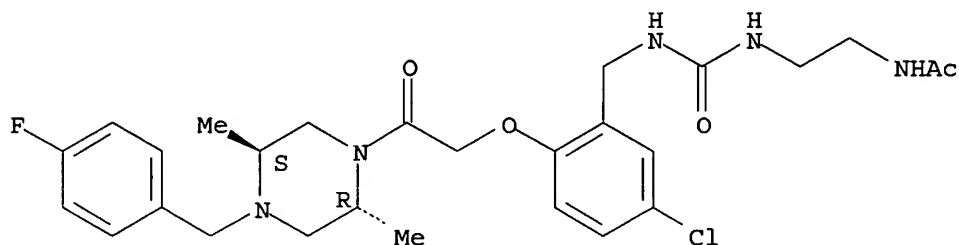
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperazines for use as pharmaceuticals for the treatment of  
inflammation and other immune disorders)

RN 364066-85-3 HCAPLUS

CN Acetamide, N-[2-[[[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl)methyl]amino]carbonyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 364066-96-6P

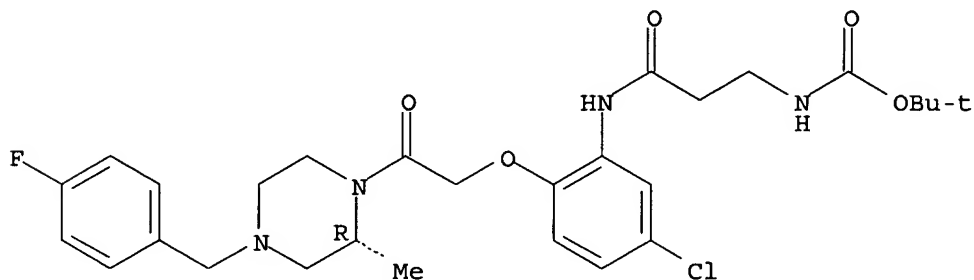
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation of piperazines for use as pharmaceuticals for the treatment of  
inflammation and other immune disorders)

RN 364066-96-6 HCAPLUS

CN Carbamic acid, [3-[[[5-chloro-2-[2-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 15 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:693319 HCAPLUS

DOCUMENT NUMBER: 135:257468

TITLE: Preparation of N-(4-thiazolylbenzoyl)-N-(cyanomethyl)-L-leucinamides and analogs as protease inhibitors

INVENTOR(S): Palmer, James T.; Setti, Eduardo L.; Tian, Zong-Qiang; Venkatraman, Shankar; Wang, Dan-Xiong

PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

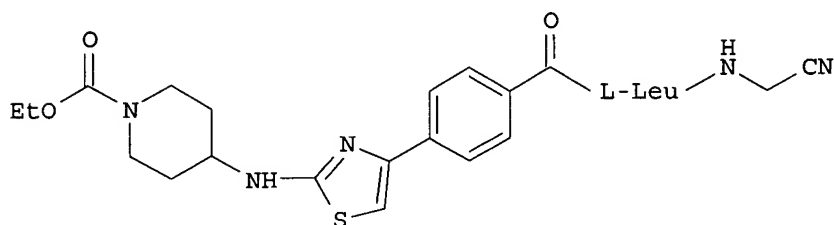
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068645	A2	20010920	WO 2001-US8332	20010314
WO 2001068645	A3	20020307		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-189694P P 20000315  
GI



AB The title compds. and their pharmaceutically acceptable salts, N-oxides, prodrugs, protected derivs., or isomers thereof were prepared as cysteine protease inhibitors. For example, stirring a solution of 4-[2-(1-tert-butoxycarbonylpiperidin-4-ylamino)thiazol-4-yl]benzoic acid (preparation given) and the MeSO<sub>3</sub>H salt of 2S-amino-N-cyanomethyl-4-methylpentanamide overnight at room temperature with PyBOP and diisopropylethylamine in DMF, followed by conversion to the Et ester, yielded I (77%). Test compds. inhibited cathepsin B, K, L, and S (no data). The invention compds. and compns. with a bisphosphonic acid and/or an estrogen receptor agonist are claimed for treating osteoporosis in post-menopausal women (no data).

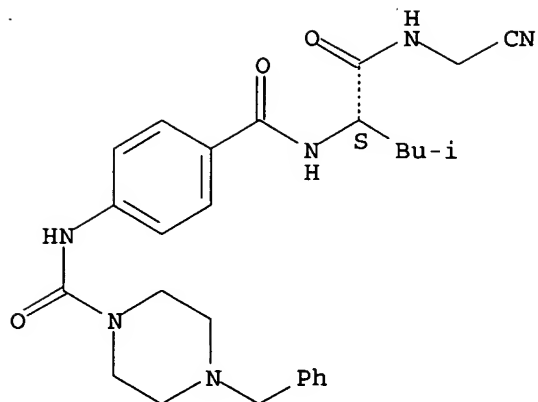
IT 294623-12-4P 294623-26-0P 361519-37-1P  
361519-43-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-thiazolylbenzoyl-N-cyanomethyl-L-leucinamides and analogs as cysteine protease inhibitors for treatment of osteoporosis)

RN 294623-12-4 HCAPLUS

CN 1-Piperazinecarboxamide, N-[4-[[[(1S)-1-[[[cyanomethyl]amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

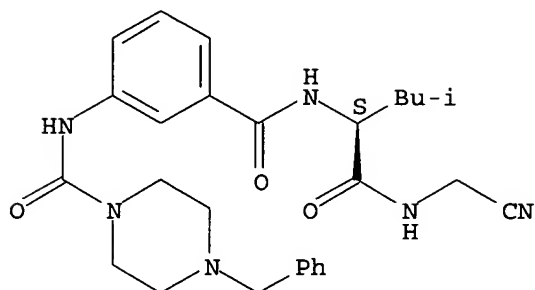
Absolute stereochemistry.



RN 294623-26-0 HCAPLUS

CN 1-Piperazinecarboxamide, N-[3-[[[(1S)-1-[[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 361519-37-1 HCAPLUS

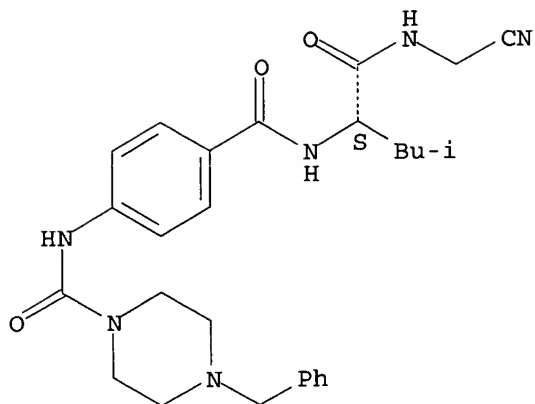
CN 1-Piperazinecarboxamide, N-[4-[[[(1S)-1-[[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-4-(phenylmethyl)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 294623-12-4

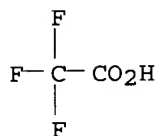
CMF C27 H34 N6 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1  
CMF C2 H F3 O2

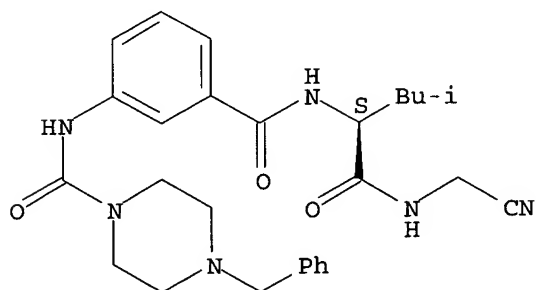


RN 361519-43-9 HCAPLUS  
CN 1-Piperazinecarboxamide, N-[3-[[[(1S)-1-[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-4-(phenylmethyl)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 294623-26-0  
CMF C27 H34 N6 O3

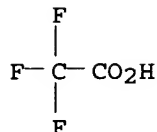
Absolute stereochemistry.



CM 2

CRN 76-05-1  
CMF C2 H F3 O2





L12 ANSWER 16 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:297641 HCAPLUS

DOCUMENT NUMBER: 134:311427

TITLE: Inhibitors of protein isoprenyl transferases

INVENTOR(S): Sebti, Said M.; Hamilton, Andrew D.; Barr, Kenneth J.; Fakhoury, Stephen A.; O'Connor, Stephen J.; Rosenberg, Saul H.; Shen, Wang; Sorensen, Bryan K.; Sullivan, Gerard M.; Wasicak, James T.; Henry, Kenneth J.; Wang, Le

PATENT ASSIGNEE(S): University of Pittsburgh, USA

SOURCE: U.S., 388 pp., Cont.-in-part of U.S. Ser. No. 852,858, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6221865	B1	20010424	US 1998-73795	19980507
PRIORITY APPLN. INFO.:			US 1995-7247P	P 19951106
			US 1996-740909	B2 19961105
			US 1997-852858	B2 19970507

OTHER SOURCE(S): MARPAT 134:311427

AB Compds. R3-Z-L1-aryl [aryl is a benzene ring having certain substituents R1, R2, R4; L1 is methylene; Z is a covalent bond; R3 is (un)substituted pyrrolidin-1-yl] were prepared as inhibitors of protein isoprenyl transferases. N-[4-(2-benzyloxymethylpyrrolidin-1-ylmethyl)-2-(2-methylphenyl)benzoyl]methionine is one of 18 compds. claimed. Syntheses of compds. of the invention are illustrated in > 100 examples and data for inhibition of farnesyltransferase are tabulated.

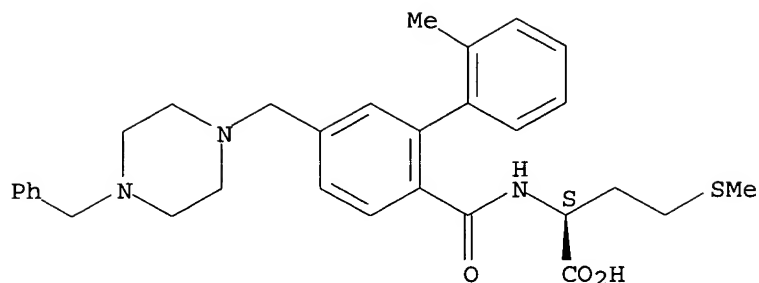
IT 215920-11-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(inhibitors of protein isoprenyl transferases)

RN 215920-11-9 HCAPLUS

CN L-Methionine, N-[[2'-methyl-5-[[4-(phenylmethyl)-1-piperazinyl]methyl][1,1'-biphenyl]-2-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 17 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:222006 HCAPLUS

DOCUMENT NUMBER: 134:252354

TITLE: Preparation of N-benzylpiperazines as antiinflammatory agents

INVENTOR(S): Bauman, John G.; Buckman, Brad O.; Ghannam, Ameen F.; Hesselgesser, Joseph E.; Horuk, Richard; Islam, Imadul; Liang, Meina; May, Karen B.; Monahan, Sean D.; Morrissey, Michael M.; Ng, Howard P.; Wei, Guo Ping; Xu, Wei; Zheng, Wei

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: U.S., 87 pp., Cont.-in-part of U.S. Ser. No. 873,599, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

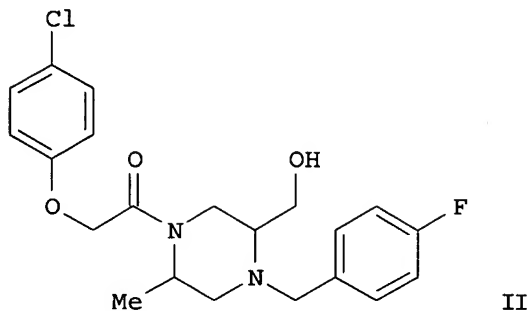
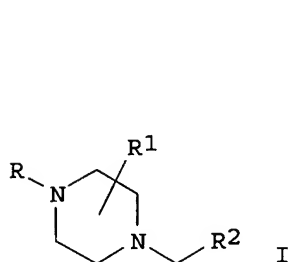
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6207665	B1	20010327	US 1998-94397	19980609
CA 2293382	AA	19981217	CA 1998-2293382	19980611
AU 9886258	A1	19981230	AU 1998-86258	19980611
AU 735462	B2	20010712		
EP 988292	A2	20000329	EP 1998-937467	19980611
EP 988292	B1	20030212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EE 9900565	A	20000615	EE 1999-565	19980611
EE 4056	B1	20030616		
TR 9903034	T2	20000621	TR 1999-9903034	19980611
JP 2002503239	T2	20020129	JP 1999-501611	19980611
EP 1254899	A2	20021106	EP 2002-90193	19980611
EP 1254899	A3	20030219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 232522	E	20030215	AT 1998-937467	19980611
EE 200200682	A	20030415	EE 2002-200200682	19980611
EE 200200683	A	20030415	EE 2002-200200683	19980611
EE 200200684	A	20030415	EE 2002-200200684	19980611
ES 2191320	T3	20030901	ES 1998-937467	19980611
IL 132398	A1	20040831	IL 1998-132398	19980611
NO 9906068	A	20000211	NO 1999-6068	19991209

MX 9911506	A	20000430	MX 1999-11506	19991210
US 6541476	B1	20030401	US 2000-713606	20001114
US 6534509	B1	20030318	US 2000-713881	20001115
US 6573266	B1	20030603	US 2000-714937	20001116
US 2002177598	A1	20021128	US 2000-726808	20001129
US 6555537	B2	20030429		
US 2003139425	A1	20030724	US 2003-347530	20030117
US 2003158205	A1	20030821	US 2003-347529	20030117
NO 2003001373	A	20000211	NO 2003-1373	20030326
PRIORITY APPLN. INFO.:			US 1997-873599	B2 19970612
			US 1998-94397	A 19980609
			EP 1998-937467	A3 19980611
			WO 1998-EP3503	W 19980611
			US 2000-714937	A3 20001116
			US 2000-726808	A1 20001129

OTHER SOURCE(S):  
GI

MARPAT 134:252354



AB Title compds. [I; R = R3Z3Z2Z1; R1 =  $\geq 1$  of halo, alkyl, aryl, etc.; R2 = (un)substituted Ph; R3 = (un)substituted carbocyclic ring system (sic) or (un)substituted heterocyclic ring system (sic); Z1 = bond, CH2, CO, etc.; Z2 = alkylene or alkylidene; Z3 = bond, O, CH2, (alkyl)imino, etc.] were prepared as chemokine inhibitors (no data). Thus, (2R,5S)-1-(4-fluorobenzyl)-2-hydroxymethyl-5-methylpiperazine was N-acylated by 4-ClC6H4OCH2COC1 to give title compound (R,R)-II.

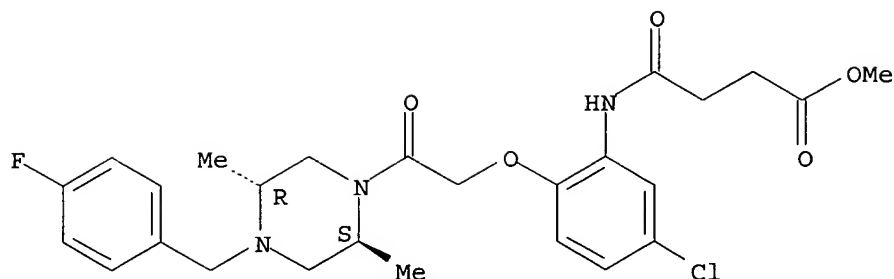
IT 217644-74-1P 217644-75-2P 217645-11-9P  
217645-12-0P 217645-13-1P 217645-14-2P  
217645-15-3P 217645-16-4P 217645-17-5P  
217645-18-6P 217645-19-7P 217645-20-0P  
217645-21-1P 217645-22-2P 217645-23-3P  
217645-25-5P 217645-29-9P 217646-95-2P  
217646-96-3P 217647-07-9P 217647-39-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-benzylpiperazines as antiinflammatory agents)

RN 217644-74-1 HCAPLUS

CN Butanoic acid, 4-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-4-oxo-, methyl ester, rel- (9CI) (CA INDEX NAME)

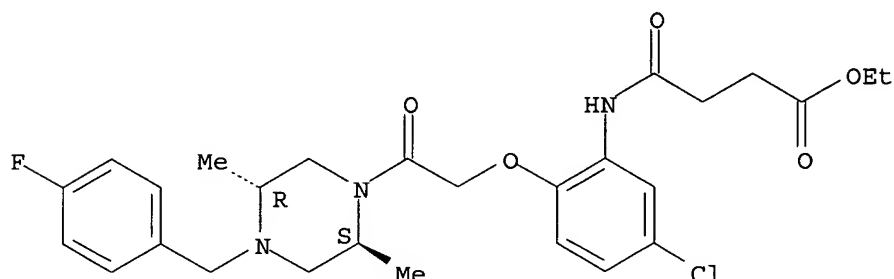
Relative stereochemistry.



RN 217644-75-2 HCAPLUS

CN Butanoic acid, 4-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-4-oxo-, ethyl ester, rel- (9CI) (CA INDEX NAME)

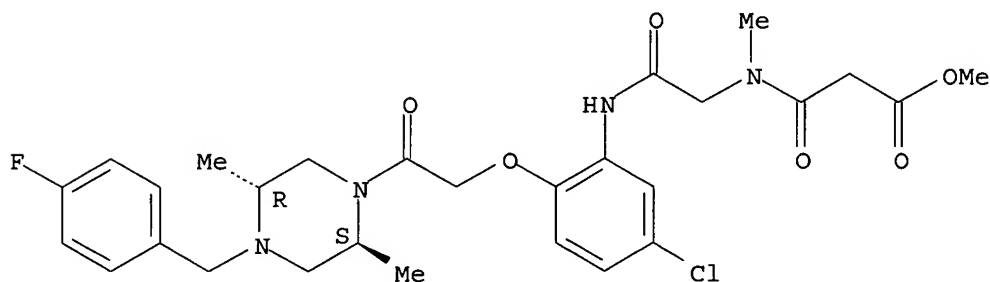
Relative stereochemistry.



RN 217645-11-9 HCAPLUS

CN Propanoic acid, 3-[[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]methylamino]-3-oxo-, methyl ester, rel- (9CI) (CA INDEX NAME)

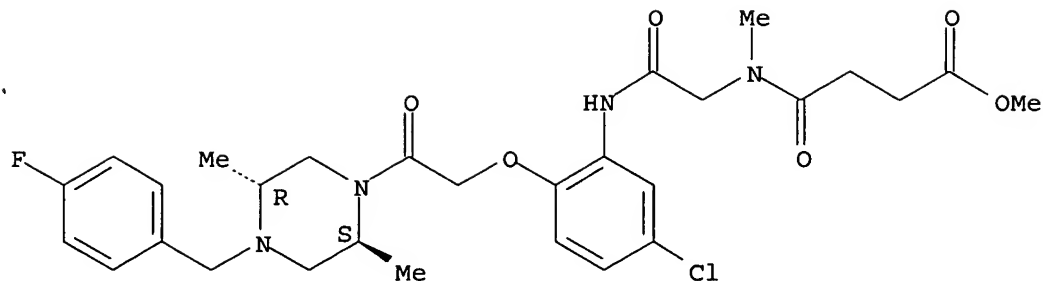
Relative stereochemistry.



RN 217645-12-0 HCAPLUS

CN Butanoic acid, 4-[[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]methylamino]-4-oxo-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

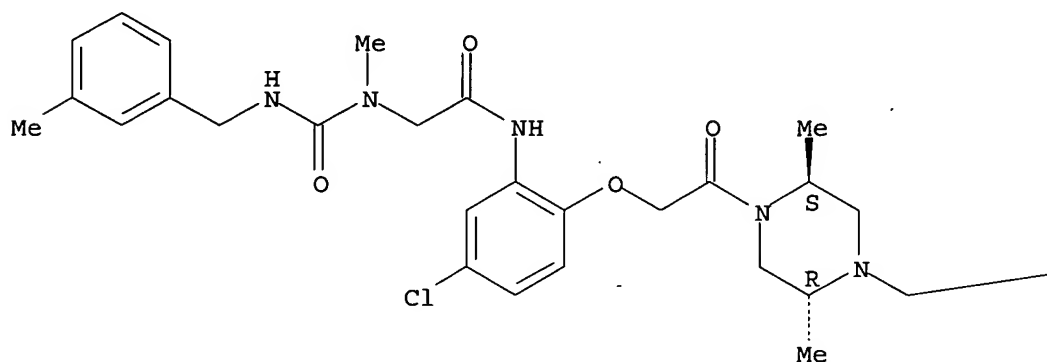


RN 217645-13-1 HCAPLUS

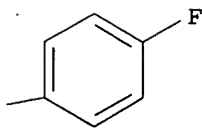
CN Acetamide, N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-2-[methyl[[[(3-methylphenyl)methyl]amino]carbonyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



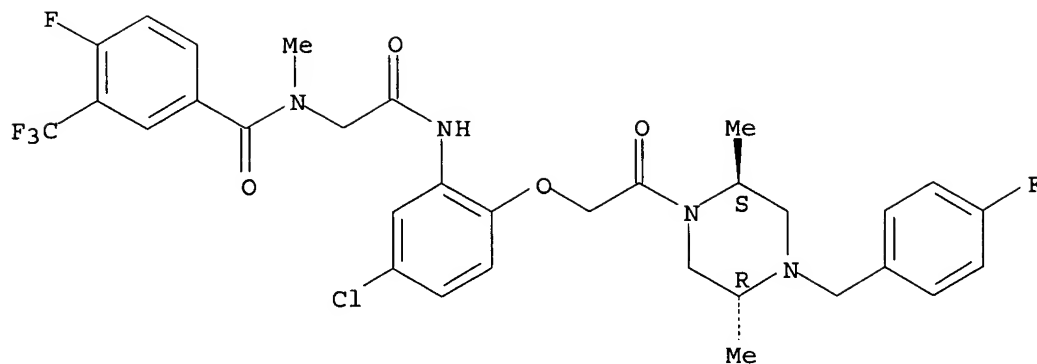
PAGE 1-B



RN 217645-14-2 HCAPLUS

CN Benzamide, N-[2-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-4-fluoro-N-methyl-3-(trifluoromethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

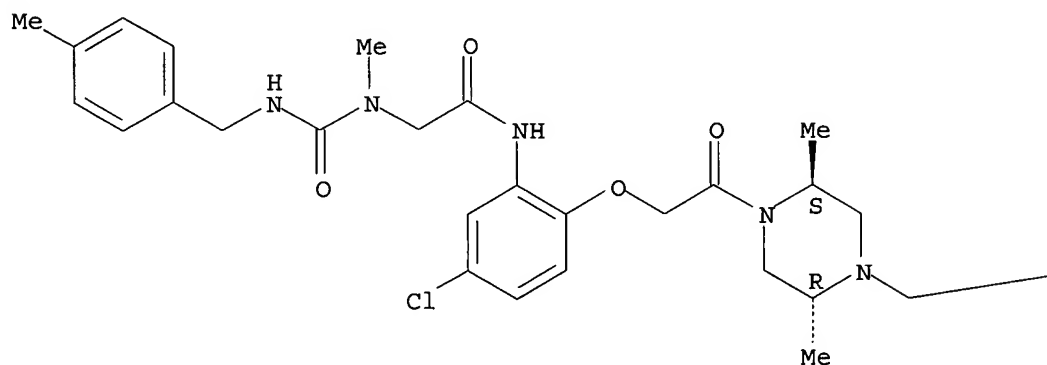


RN 217645-15-3 HCAPLUS

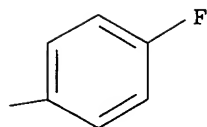
CN Acetamide, N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-2-[methyl[[[(4-methylphenyl)methyl]amino]carbonyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



PAGE 1-B

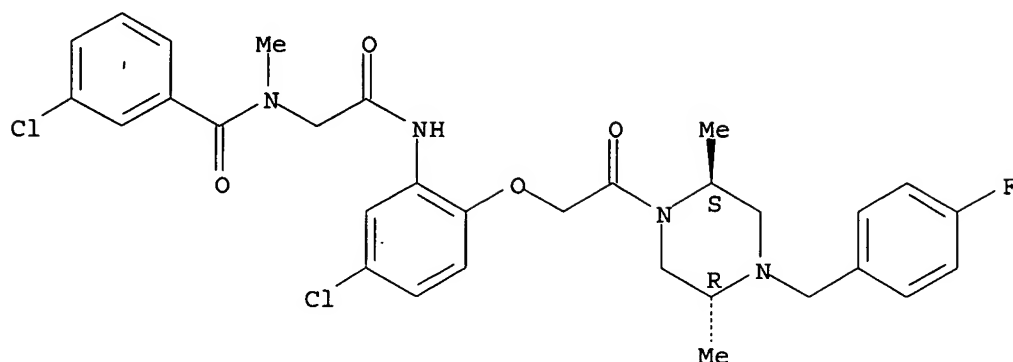


RN 217645-16-4 HCAPLUS

CN Benzamide, 3-chloro-N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-

2-oxoethyl]-N-methyl-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

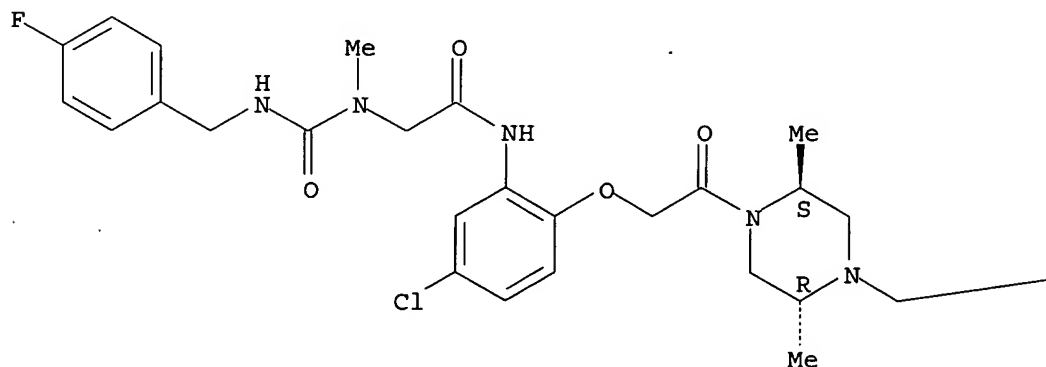


RN 217645-17-5 HCAPLUS

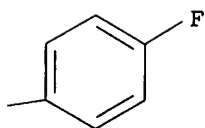
CN Acetamide, N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-2-[[[(4-fluorophenyl)methyl]amino]carbonyl]methylamino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



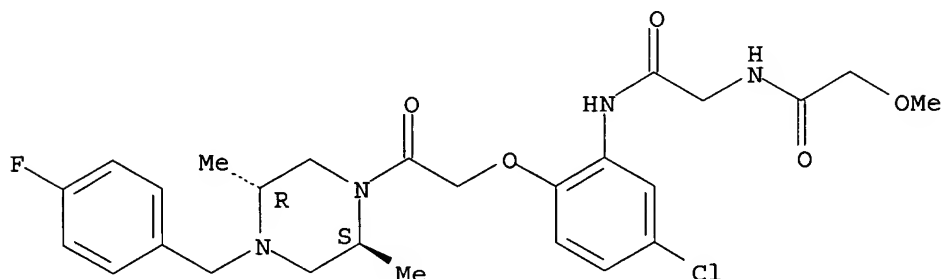
PAGE 1-B



RN 217645-18-6 HCAPLUS

CN Acetamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

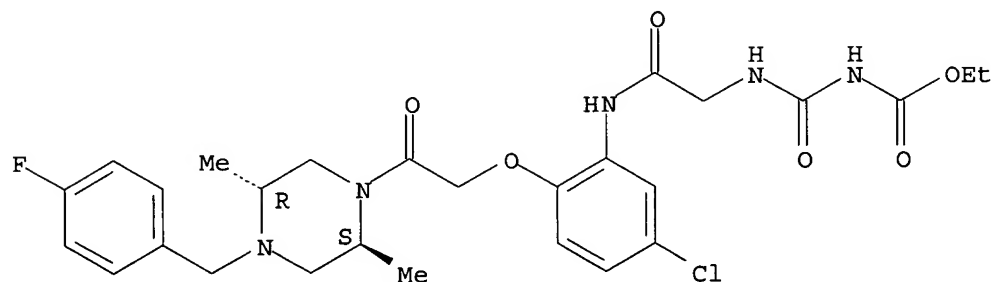
Relative stereochemistry.



RN 217645-19-7 HCAPLUS

CN Carbamic acid, [[[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]amino]carbonyl]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

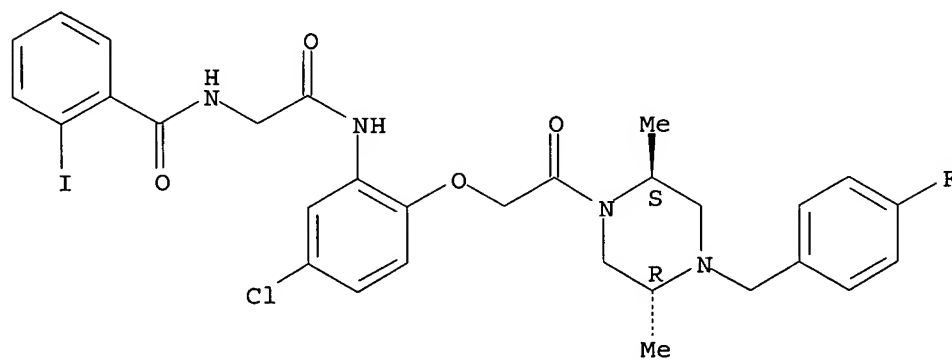
Relative stereochemistry.



RN 217645-20-0 HCAPLUS

CN Benzamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-2-iodo-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

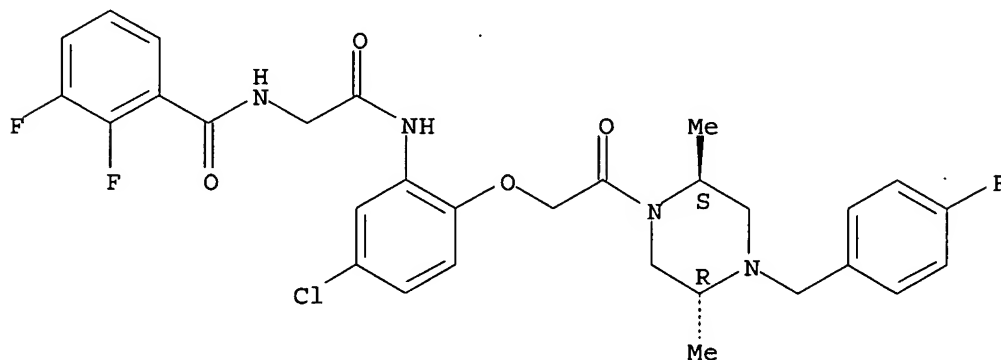




RN 217645-21-1 HCAPLUS

CN Benzamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-2,3-difluoro-, rel- (9CI) (CA INDEX NAME)

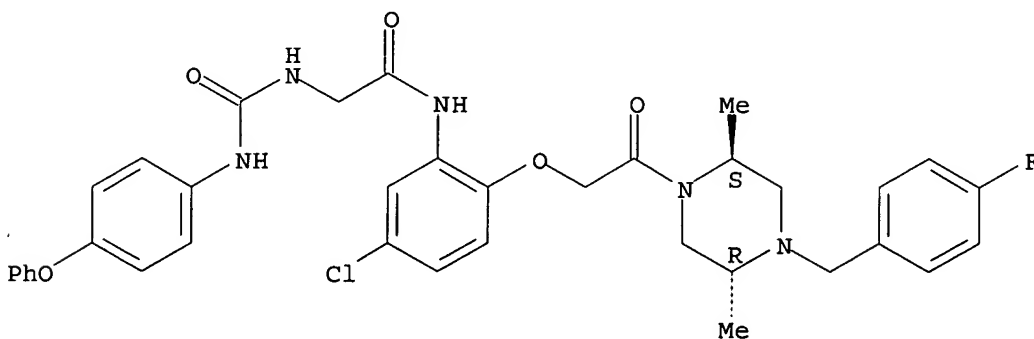
Relative stereochemistry.



RN 217645-22-2 HCAPLUS

CN Acetamide, N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-2-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-, rel- (9CI) (CA INDEX NAME)

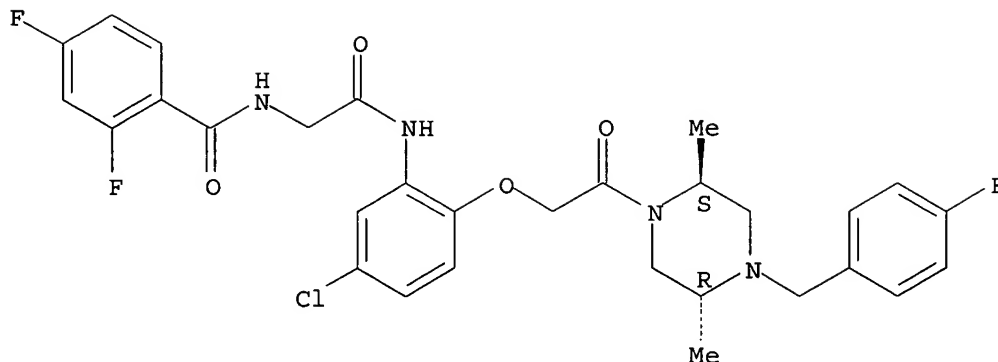
Relative stereochemistry.



RN 217645-23-3 HCAPLUS

CN Benzamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-2,4-difluoro-, rel- (9CI) (CA INDEX NAME)

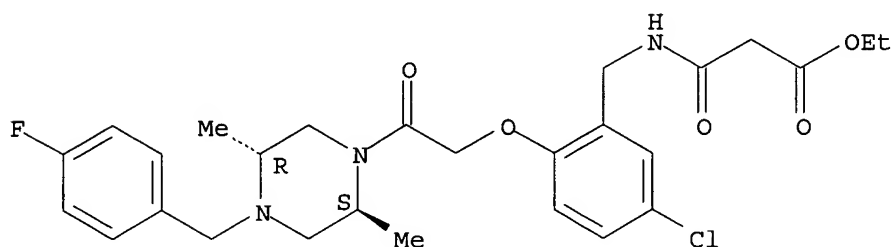
Relative stereochemistry.



RN 217645-25-5 HCAPLUS

CN Propanoic acid, 3-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]amino]-3-oxo-, ethyl ester, rel- (9CI) (CA INDEX NAME)

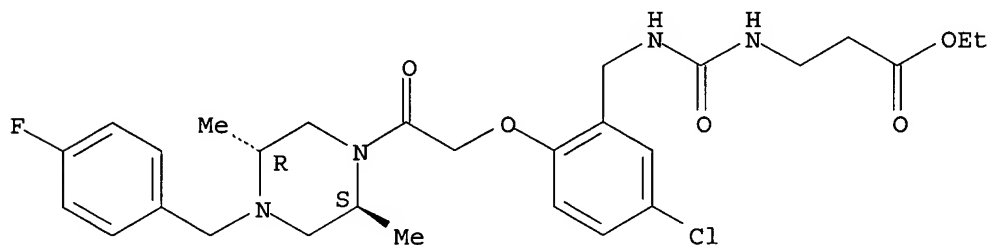
Relative stereochemistry.



RN 217645-29-9 HCAPLUS

CN  $\beta$ -Alanine, N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]amino]carbonyl]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

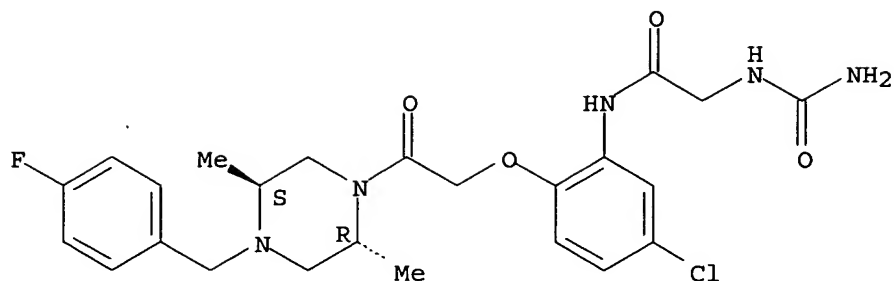
Relative stereochemistry.



RN 217646-95-2 HCAPLUS

CN Acetamide, 2-[(aminocarbonyl)amino]-N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-, rel- (9CI) (CA INDEX NAME)

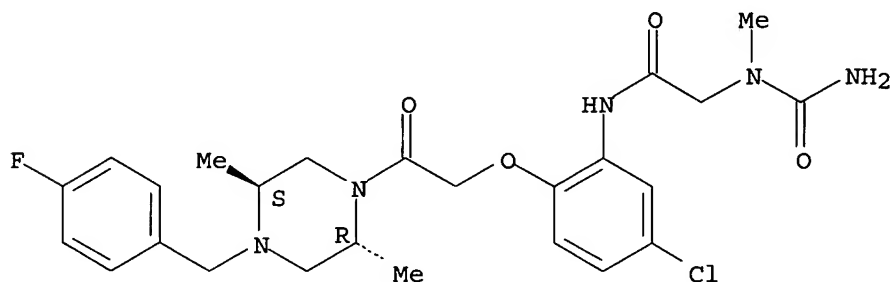
Relative stereochemistry.



RN 217646-96-3 HCAPLUS

CN Acetamide, 2-[(aminocarbonyl)methylamino]-N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-, rel- (9CI) (CA INDEX NAME)

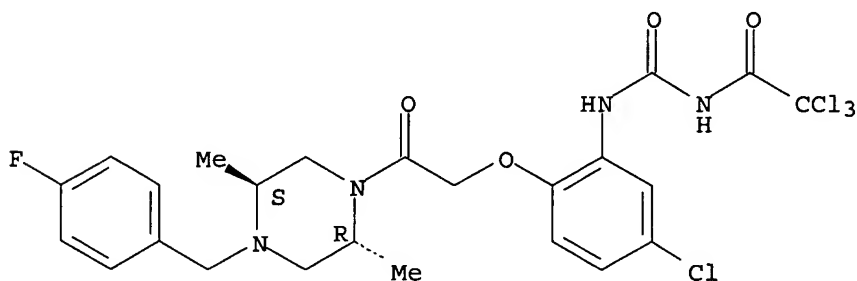
Relative stereochemistry.



RN 217647-07-9 HCAPLUS

CN Acetamide, 2,2,2-trichloro-N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]-, rel- (9CI) (CA INDEX NAME)

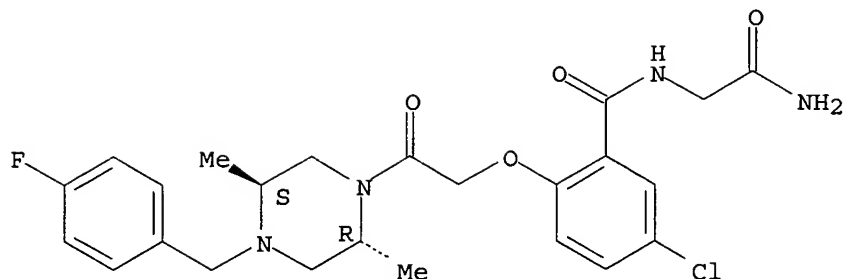
Relative stereochemistry.



RN 217647-39-7 HCAPLUS

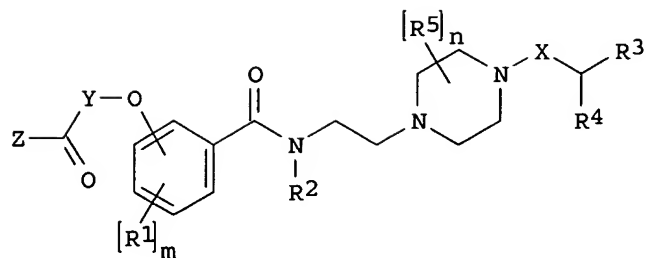
CN Benzamide, N-(2-amino-2-oxoethyl)-5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

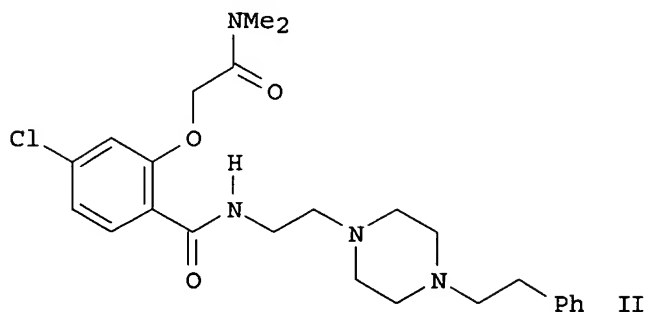


L12 ANSWER 18 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2001:31485 HCAPLUS  
DOCUMENT NUMBER: 134:86282  
TITLE: Preparation of piperazine derivatives as modulators of  
chemokine receptor activity  
INVENTOR(S): Baxter, Andrew John Gilby; Brough, Stephen John;  
Kindon, Nicholas David; McInally, Thomas; Roberts,  
Bryan  
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK  
SOURCE: PCT Int. Appl., 65 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002381	A1	20010111	WO 2000-GB2470	20000627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1196404	A1	20020417	EP 2000-942220	20000627
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JP 2003503488	T2	20030128	JP 2001-507819	20000627
US 6562825	B1	20030513	US 2000-640398	20000817
PRIORITY APPLN. INFO.:			SE 1999-2551	A 19990702
			WO 2000-GB2470	W 20000627
OTHER SOURCE(S):	MARPAT	134:86282		
GI				



I



II

AB The title compds. [I; R1 = halo, alkyl, alkoxy, etc.; m = 0-2; R2 = H, alkyl; R3, R4 = H, alkyl, (un)substituted Ph; R5 = H, alkyl; n = 0-4; X = a bond, alkyl; Y = alkyl; Z = OH, NR6R7; R6, R7 = H, alkyl, unsatd. alkyl; NR6R7 = 3-8 membered (un)substituted (un)saturated azacyclic ring system optionally incorporating one or two further heteroatoms selected from N, O and S] and their salts, useful in therapy, especially for the treatment of chemokine receptor related diseases and conditions (no data), were prepared E.g., a multi-step synthesis of the title compound II was given.

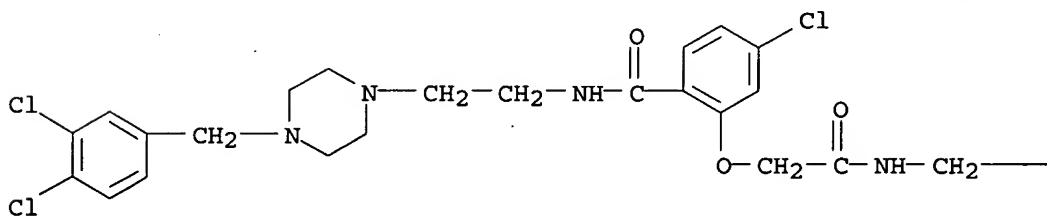
IT 318257-26-0P 318257-41-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of piperazine derivs. as modulators of chemokine receptor activity)

RN 318257-26-0 HCAPLUS

CN Glycine, N-[[5-chloro-2-[[[2-[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]ethyl]amino]carbonyl]phenoxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

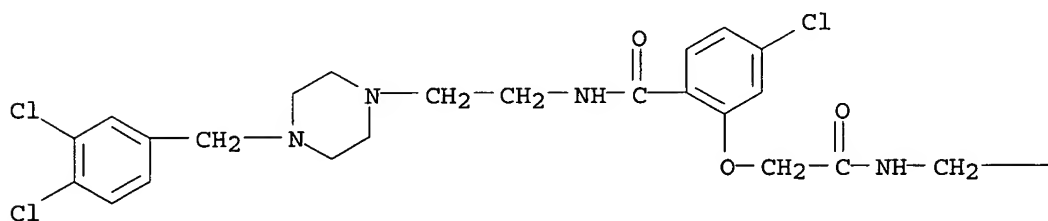


PAGE 1-B

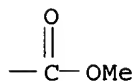
—CO<sub>2</sub>H

RN 318257-41-9 HCAPLUS  
 CN Glycine, N-[[5-chloro-2-[[[2-[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]ethyl]amino]carbonyl]phenoxy]acetyl]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 19 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2000:666701 HCAPLUS  
 DOCUMENT NUMBER: 133:252050  
 TITLE: Preparation of novel N-cyanomethyl amide compounds and compositions as protease inhibitors to treat osteoporosis  
 INVENTOR(S): Bryant, Clifford M.; Palmer, James T.; Rydzewski, Robert M.; Setti, Eduardo L.; Tian, Zong-Qiang; Venkatraman, Shankar; Wang, Dan-Xiong  
 PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 155 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000055126	A2	20000921	WO 2000-US6837	20000315
WO 2000055126	A3	20010222		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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EP 1161415	A2	20011212	EP 2000-916375	20000315
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TR 200103337	T2	20020321	TR 2001-200103337	20000315
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US 6455502	B1	20020924	US 2000-526090	20000315
TR 200201874	T2	20021021	TR 2002-200201874	20000315
US 6476026	B1	20021105	US 2000-526485	20000315
JP 2002539192	T2	20021119	JP 2000-605557	20000315
EE 200100487	A	20030217	EE 2001-487	20000315
AU 769736	B2	20040205	AU 2000-37486	20000315
PT 1178958	T	20040730	PT 2000-916343	20000315
EP 1452522	A2	20040901	EP 2004-75486	20000315
EP 1452522	A3	20050209		
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ZA 2001007494	A	20020911	ZA 2001-7494	20010911
ZA 2001007495	A	20020911	ZA 2001-7495	20010911
NO 2001004484	A	20011026	NO 2001-4484	20010914
BG 106013	A	20020531	BG 2001-106013	20011012
HR 2001000737	A1	20021031	HR 2001-737	20011012
US 2002086996	A1	20020704	US 2001-17851	20011214
US 6593327	B2	20030715		
US 2003096796	A1	20030522	US 2002-205600	20020724
US 2003119788	A1	20030626	US 2002-241001	20020909
US 2004147745	A1	20040729	US 2004-758893	20040115
PRIORITY APPLN. INFO.:				
			US 1999-124420P	P 19990315
			EP 2000-916343	A3 20000315
			US 2000-526090	A1 20000315
			US 2000-526485	A3 20000315
			WO 2000-US6837	W 20000315
			US 2002-205600	B1 20020724

OTHER SOURCE(S): MARPAT 133:252050

AB Title compds. [R1R2NCR3R4CN; R1 = R11R7NCR5R9X1, R11R8NCR6R10X2NR7CR5R9CX1; X1, X2 independently = CO, CH2SO2; R5, R6 independently = H, C1-6alkyl; R7, R8 independently = H, C1-6alkyl; R9, R10 independently = (un)substituted-C1-6alkyl; R9-R7 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R10-R8 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R5-R9 = C3-8cycloalkylene, C3-8heterocycloalkylene; R10-R6 = C3-8cycloalkylene, C3-8heterocycloalkylene; R11 = X4X5R18; X4 = CO, COCO, SO2; X5 = bond, O, NH; R18 = C1-6alkyl; R2 = H, C1-6alkyl; R3 = H, C1-6alkyl; R4 = CN, COOH, COOC1-6alkyl; R2-R4 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R4-R3 = C3-8cycloalkylene, C3-8heterocycloalkylene], N-oxide, prodrug, isomers,

pharmaceutically acceptable salts, and composition are prepared as therapeutically effective estrogen receptor agonist. Title compds. are claimed in treating osteoporosis in post-menopausal woman in which cathepsin K activity contributes to the pathol. and symptomatol. of the disease. Thus, the title compound (S)-C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>OCONHCH(CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>)CONHCH<sub>2</sub>CN was prepared

IT 294623-13-5P 294623-27-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of novel N-cyanomethyl amides and compns. as protease inhibitors)

RN 294623-13-5 HCAPLUS

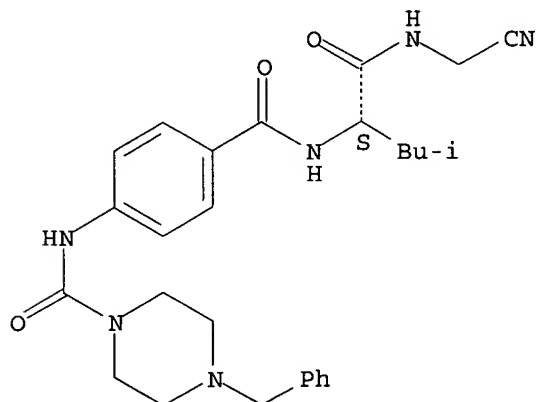
CN 1-Piperazinecarboxamide, N-[4-[[[(1S)-1-[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-4-(phenylmethyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 294623-12-4

CMF C27 H34 N6 O3

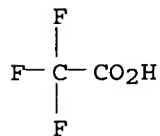
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 294623-27-1 HCAPLUS

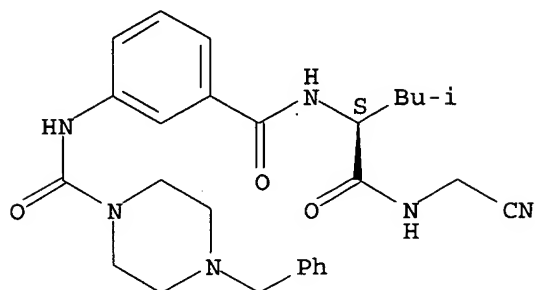
CN 1-Piperazinecarboxamide, N-[3-[[[(1S)-1-[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-4-(phenylmethyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)



CM 1

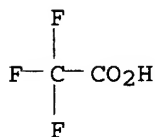
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CMF C27 H34 N6 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1  
CMF C2 H F3 O2



L12 ANSWER 20 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2000:666700 HCAPLUS  
 DOCUMENT NUMBER: 133:252170  
 TITLE: Preparation of novel N-cyanomethyl amides as protease inhibitors  
 INVENTOR(S): Bryant, Clifford M.; Bunin, Barry A.; Kraynack, Erica A.; Patterson, John W.  
 PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 137 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055125	A2	20000921	WO 2000-US6747	20000315
WO 2000055125	A3	20010426		

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2368122	AA	20000921	CA 2000-2368122	20000315
BR 2000009042	A	20011226	BR 2000-9042	20000315
EP 1178958	A2	20020213	EP 2000-916343	20000315
EP 1178958	B1	20040218		

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TR 200103390	T2	20020521	TR 2001-200103390	20000315
US 6455502	B1	20020924	US 2000-526090	20000315
TR 200201874	T2	20021021	TR 2002-200201874	20000315
US 6476026	B1	20021105	US 2000-526485	20000315
JP 2002539191	T2	20021119	JP 2000-605556	20000315
EE 200100485	A	20030217	EE 2001-485	20000315
NZ 514234	A	20040227	NZ 2000-514234	20000315
AT 259782	E	20040315	AT 2000-916343	20000315
AU 774827	B2	20040708	AU 2000-37461	20000315
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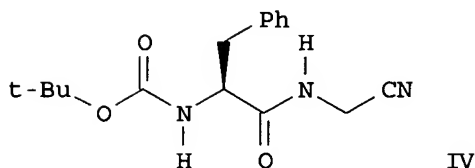
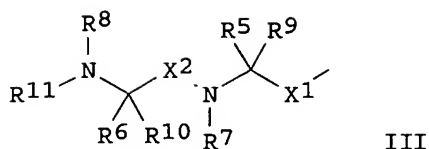
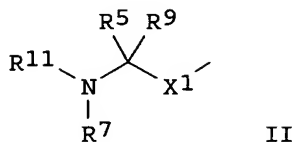
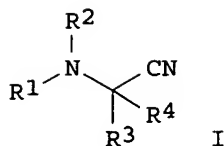
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ZA 2001007495	A	20020911	ZA 2001-7495	20010911
NO 2001004485	A	20011105	NO 2001-4485	20010914
BG 106003	A	20020628	BG 2001-106003	20011010
HR 2001000738	A1	20021231	HR 2001-738	20011012
US 2002086996	A1	20020704	US 2001-17851	20011214
US 6593327	B2	20030715		
US 2003096796	A1	20030522	US 2002-205600	20020724
HK 1044755	A1	20041217	HK 2002-105942	20020813
US 2003119788	A1	20030626	US 2002-241001	20020909
US 2004147745	A1	20040729	US 2004-758893	20040115

PRIORITY APPLN. INFO.:

US 1999-124420P	P	19990315
EP 2000-916343	A3	20000315
US 2000-526090	A1	20000315
US 2000-526485	A3	20000315
WO 2000-US6747	W	20000315
US 2002-205600	B1	20020724

OTHER SOURCE(S): MARPAT 133:252170  
 GI



AB The title compds. [I; R1 = II, III (wherein X1, X2 = CO, CH<sub>2</sub>SO<sub>2</sub>; R5, R6 = H, alkyl; R7, R8 = H, alkyl, etc.; R9, R10 = alkyl optionally substituted with CN, halo, NO<sub>2</sub>, etc.; R11 = X<sub>5</sub>X<sub>6</sub>R<sub>18</sub>; X<sub>5</sub> = CO, COCO, SO<sub>2</sub>; X<sub>6</sub> = a bond, O, NH, N(alkyl); R<sub>18</sub> = alkyl optionally substituted with CN, halo, NO<sub>2</sub>, etc.); R2 = H, alkyl, etc.; R3 = H, alkyl, etc.; R4 = H, alkyl optionally substituted with CN, halo, NO<sub>2</sub>, etc.; R4 and R2 taken together form trimethylene, tetramethylene, phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; R4 and R3 together with the carbon atom to which both are attached form cycloalkylene, heterocycloalkylene], useful for treating diseases associated with cysteine protease activity, particularly diseases associated with activity of cathepsins B, K, L or S such as inflammation and asthma, were prepared and formulated. Thus, reacting 2(S)-tert-butoxycarbonylamino-3-phenylpropionic acid with aminoacetonitrile.HCl in the presence of Et<sub>3</sub>N in DMF and MeCN afforded the amide (1S)-IV. Biol. data for compds. I were given.

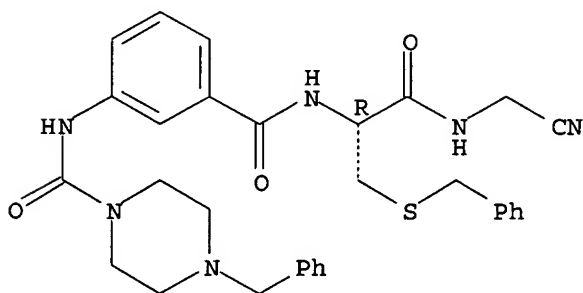
IT 294641-81-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of novel N-cyanomethyl amides as protease inhibitors)

RN 294641-81-9 HCAPLUS

CN 1-Piperazinecarboxamide, N-[3-[[[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[[(phenylmethyl)thio]methyl]ethyl]amino]carbonyl]phenyl]-4-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 21 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:441775 HCAPLUS

DOCUMENT NUMBER: 133:74330

TITLE: Preparation of peptides useful in the treatment of inflammatory diseases

INVENTOR(S): Armour, Duncan Robert; Brown, David; Congreave, Miles Stuart; Gore, Paul Martin; Green, Darren Victor Steven; Holman, Stuart; Jack, Torquil Iain Maclean; Keeling, Steven Philip; Mason, Andrew Murtrie; Morriss, Karen; Ramsden, Nigel Grahame; Ward, Peter

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 88 pp.

CODEN: PIXXD2

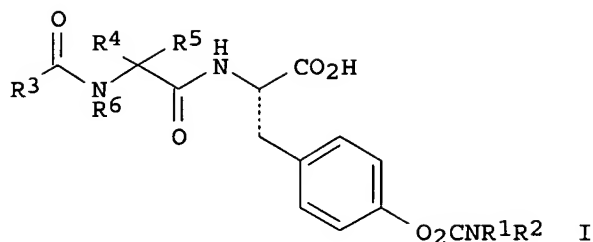
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037444	A1	20000629	WO 1999-EP10000	19991216
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AT 273954	E	20040915	AT 1999-964583	19991216
ES 2226488	T3	20050316	ES 1999-964583	19991216
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US 6867192	B1	20050315	US 2001-868395	20010906
PRIORITY APPLN. INFO.:			GB 1998-28074	A 19981218
			WO 1999-EP10000	W 19991216
OTHER SOURCE(S):	MARPAT 133:74330			
GI				



AB Peptides I [ $R^1$ ,  $R^2$  = (un)substituted alkyl, cycloalkyl, alkylcycloalkyl, or aryl- or aryloxy-C1-3-n-alkyl or  $R^1R^2N$  = (un)substituted or (un)benzo-fused pyrrolidinyl, piperidinyl, piperazinyl, thiomorpholinyl, morpholinyl, or azepinyl;  $R^3$  = guanidinoalkyl, -alkenyl, or -alkynyl, amino-, carbamoyl-, acyl-, ureido-, carboxy-, aryl-, aryloxy- or (un)substituted heterocyclyl-substituted alkyl, arylalkoxy, aryloxoalkyl;  $R^4$  = H, (un)substituted alkyl;  $R^5$  = H or  $R^4R^5C$  = cycloalkyl;  $R^6$  = H or  $R^4R^6$  together with the N and C atoms to which they are attached form a pyrrolidine ring] were prepared for the treatment of inflammatory diseases. Thus, (2S)-3-[4-[[[(4-acetyl-1-piperazinyl)carbonyl]oxy]phenyl]-2-[[[(2S)-2-[[2-(2-tert-butylphenoxy)acetyl]amino]-4-methylpentanoyl]amino]propanoic acid was prepared and showed  $pIC_{50}$  = 8.49 in the Jurkat J6/VCAM-1 adhesion assay.

IT 278598-33-7P 278598-40-6P 278598-41-7P  
278598-42-8P 278598-43-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

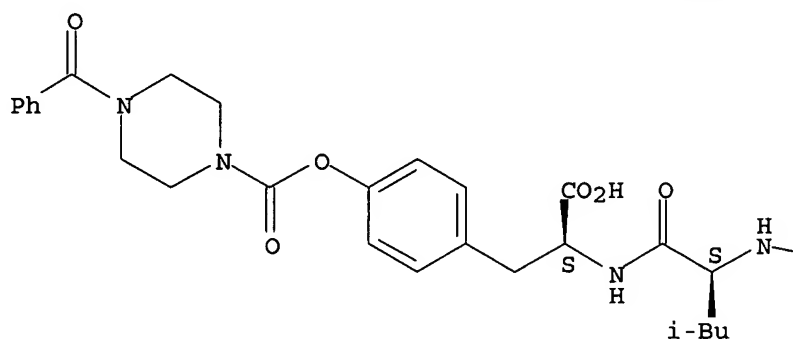
(preparation of peptides useful in the treatment of inflammatory diseases)

RN 278598-33-7 HCAPLUS

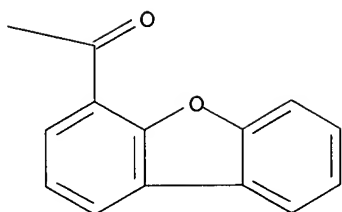
CN L-Tyrosine, N-(4-dibenzofuranylcarbonyl)-L-leucyl-, 4-benzoyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

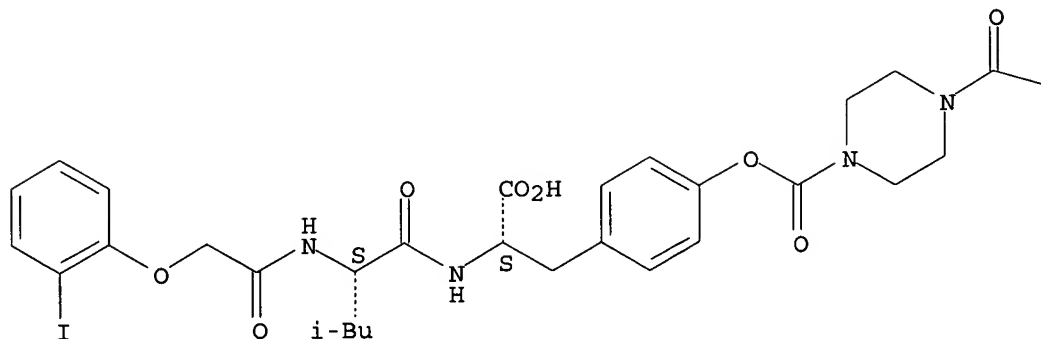


RN 278598-40-6 HCAPLUS

CN L-Tyrosine, N-[(2-iodophenoxy)acetyl]-L-leucyl-, 4-benzoyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

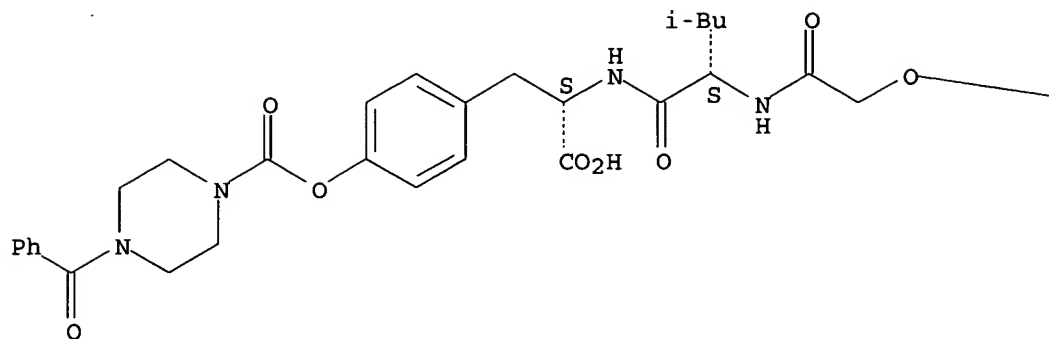
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RN 278598-41-7 HCAPLUS

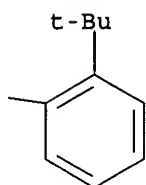
CN L-Tyrosine, N-[[2-(1,1-dimethylethyl)phenoxy]acetyl]-L-leucyl-, 4-benzoyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



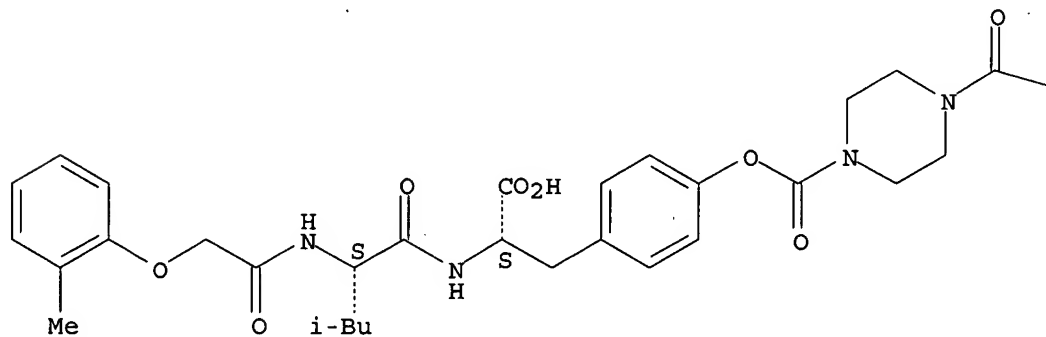
PAGE 1-B



RN 278598-42-8 HCAPLUS  
 CN L-Tyrosine, N-[(2-methylphenoxy)acetyl]-L-leucyl-, 4-benzoyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



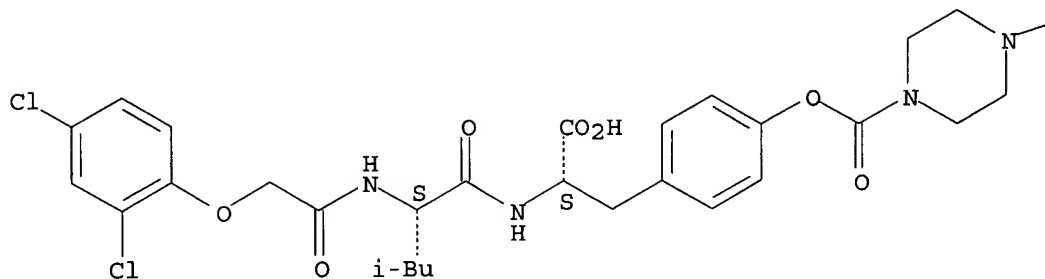
PAGE 1-B



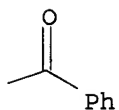
RN 278598-43-9 HCAPLUS  
 CN L-Tyrosine, N-[(2,4-dichlorophenoxy)acetyl]-L-leucyl-, 4-benzoyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 278597-86-7P

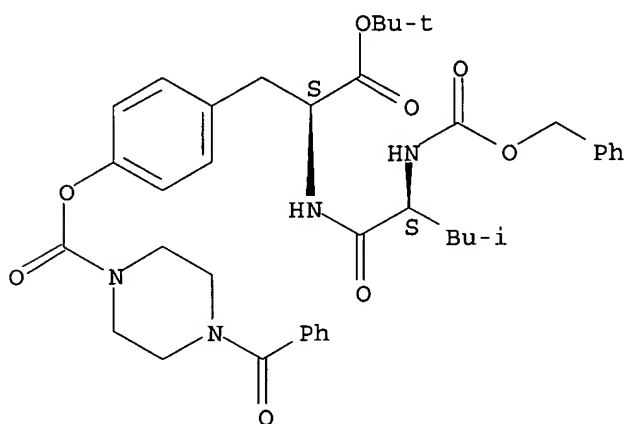
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptides useful in the treatment of inflammatory diseases)

RN 278597-86-7 HCAPLUS

CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-L-leucyl-, 1,1-dimethylethyl ester, 4-benzoyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 22 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:161119 HCAPLUS

DOCUMENT NUMBER: 132:203174

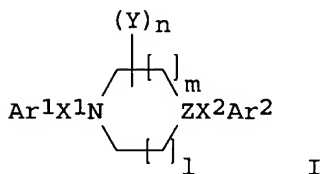
TITLE: Inhibitors of p38- $\alpha$  kinase, preparation thereof,



and therapeutic use  
 INVENTOR(S): Goehring, R. Richard; Luedtke, Gregory R.; Mavunkel, Babu J.; Chakravarty, Sarvajit; Dugar, Sundeep; Schreiner, George F.; Liu, David Y.; Lewicki, John A.  
 PATENT ASSIGNEE(S): Scios Inc., USA  
 SOURCE: PCT Int. Appl., 75 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012074	A2	20000309	WO 1999-US19845	19990827
WO 2000012074	A3	20000831		
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, EE, GE, HU, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2342251	AA	20000309	CA 1999-2342251	19990827
AU 9957936	A1	20000321	AU 1999-57936	19990827
AU 772477	B2	20040429		
EP 1107758	A2	20010620	EP 1999-945316	19990827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9913654	A	20011127	BR 1999-13654	19990827
JP 2002523448	T2	20020730	JP 2000-567192	19990827
PRIORITY APPLN. INFO.:				
			US 1998-98219P	P 19980828
			US 1999-125343P	P 19990319
			WO 1999-US19845	W 19990827

OTHER SOURCE(S): MARPAT 132:203174  
 GI



AB Methods are provided for treating conditions mediated by p38- $\alpha$  kinase using compds. I (Z = N, CR1; R1 = noninterfering substituent; X1, X2 = linker; Ar1, Ar2 = (un)substituted C1-20 hydrocarbyl (at least one of Ar1 and Ar2 = (un)substituted aryl), with proviso that when X2 = CH2 or an isostere thereof, X1 = CO or an isostere thereof, and Ar2 = (un)substituted Ph, Ar1 is other than (un)substituted indolyl, benzimidazolyl or benzotriazolyl, and wherein (un)substituted Ph is not (un)substituted indolyl, benzimidazolyl, or benzotriazolyl; Y = noninterfering substituent; n, m = 0-4; l = 0-3) or a pharmaceutically acceptable salt or pharmaceutical composition thereof. Preparation of compds. is described. Compds. of the invention may be used to treat p38- $\alpha$

kinase-mediated conditions.

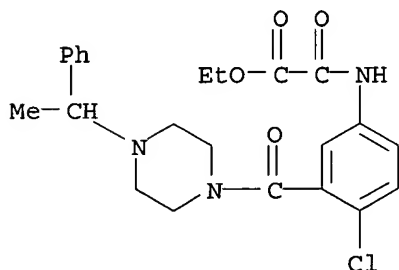
IT 260427-74-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(p38- $\alpha$  kinase inhibitors, preparation, and therapeutic use)

RN 260427-74-5 HCAPLUS

CN Acetic acid, [[4-chloro-3-[[4-(1-phenylethyl)-1-piperazinyl]carbonyl]phenyl]amino]oxo-, ethyl ester (9CI) (CA INDEX NAME)



L12 ANSWER 23 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:43346 HCAPLUS

DOCUMENT NUMBER: 132:93337

TITLE: Preparation of benzylpiperazine derivatives as delta opioid receptor agonists

INVENTOR(S): Maw, Graham Nigel; Middleton, Donald Stuart

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 289 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

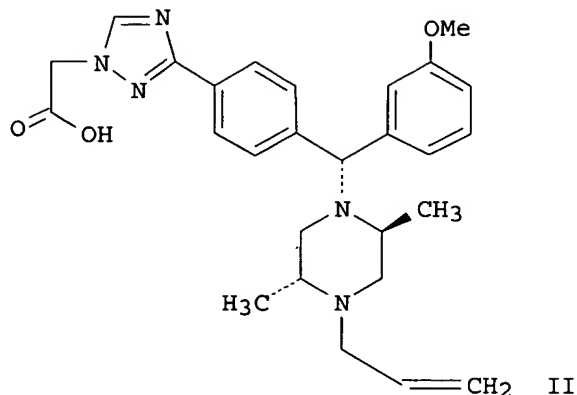
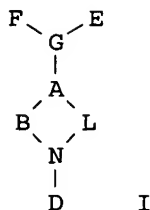
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000016984	A2	20000118	JP 1999-58364	19990305
JP 3416069	B2	20030616		
US 6200978	B1	20010313	US 1999-261540	19990303
CA 2263957	C	20031007	CA 1999-2263957	19990303
CA 2263957	AA	19990905		
BR 9917527	A	20020723	BR 1999-17527	19990305
PRIORITY APPLN. INFO.:			GB 1998-4734	A 19980305
OTHER SOURCE(S):	MARPAT	132:93337		

GI



AB Title compds [I; A = N, CX; X = H, c1-4 alkyl; G = CY; Y = H, c1-4alkyl; B = c1-4 hydrocarbonyl; A, B, L, N constitute 5-7 atoms ring; D = H, c1-10 hydrocarbonyl; D linked to B or L forming 5-7 membered-ring; E = OH substituted Ph, c1-4 alkoxy, NH<sub>2</sub>SO<sub>2</sub>c1-4alkylene; F = aryl, heterocyclyl (exclude tetrazolyl)], pharmaceutically acceptable salt, solvate, and stereoisomers are prepared and tested as delta opioid receptor agonists and claimed useful in the manufacture of pharmaceutical composition, including

method

comprising administering to a subject an effective amount of a title compound, for preventing or in treatment of inflammation diseases such as arthritis, psoriasis, asthma, inflammatory bowel disease, disorders of respiratory function, gastro-intestinal disorders, such as functional bowel disease, functional GI disorders (irritable bowel syndrome), functional diarrhea, functional distension, functional pain, non-ulcerogenic dyspepsia, or others associated with disorders of motility or secretion, urogenital tract disorders such as incontinence, as analgesics for treating pain including non-somatic pain, or as immunosuppressants to prevent rejection in organ transplant and skin graft. The title compound II was prepared

IT 253800-98-5P 253800-99-6P 253801-00-2P

253801-27-3P 253801-28-4P 253801-29-5P

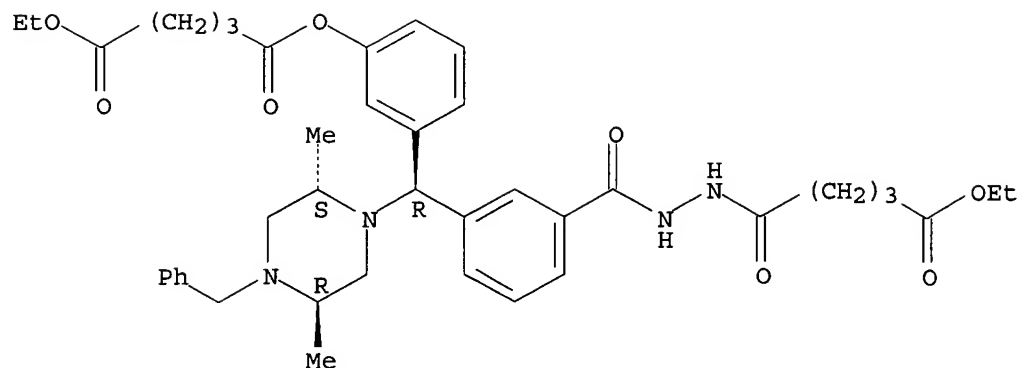
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzylpiperazine derivs. as delta opioid receptor agonists)

RN 253800-98-5 HCAPLUS

CN Pentanedioic acid, monoethyl ester, 2-[3-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl][3-[(5-ethoxy-1,5-dioxopentyl)oxy]phenyl]methyl]benzoyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

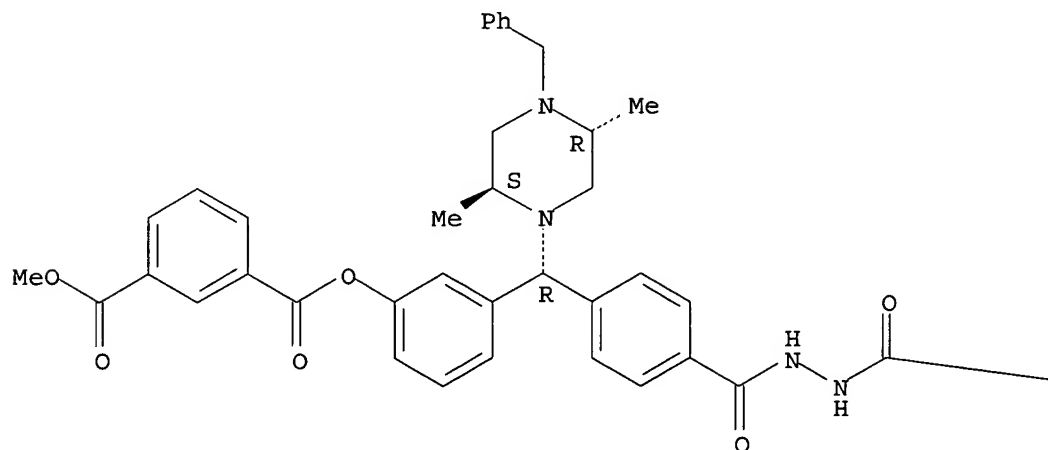


RN 253800-99-6 HCAPLUS

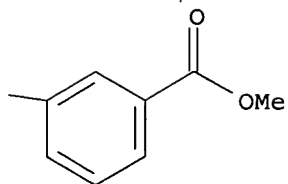
CN 1,3-Benzenedicarboxylic acid, monomethyl ester, 2-[4-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl] [3-[[3-(methoxycarbonyl)benzoyl]oxy]phenyl]methyl]benzoyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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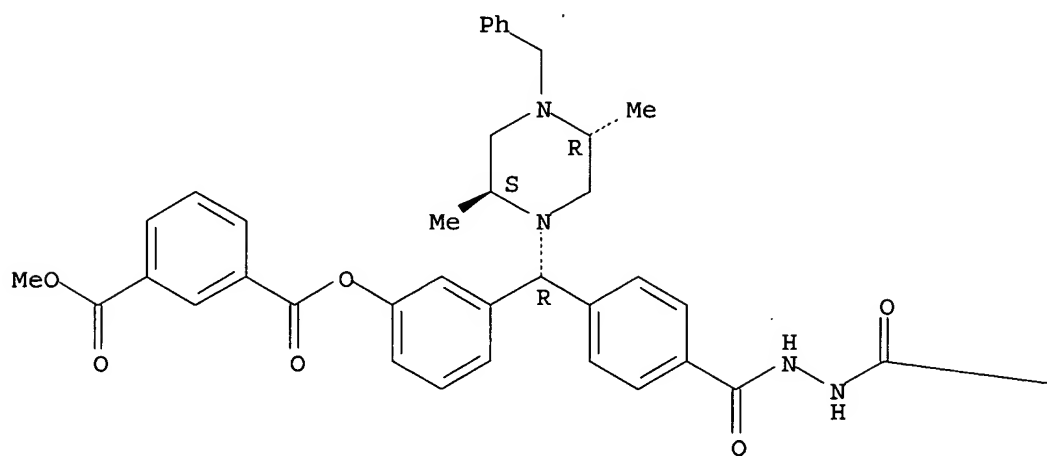


RN 253801-00-2 HCAPLUS

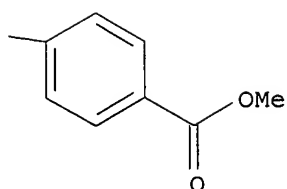
CN 1,3-Benzenedicarboxylic acid, 3-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl][4-[[2-[4-(methoxycarbonyl)benzoyl]hydrazino]carbonyl]phenyl]methyl]phenyl methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



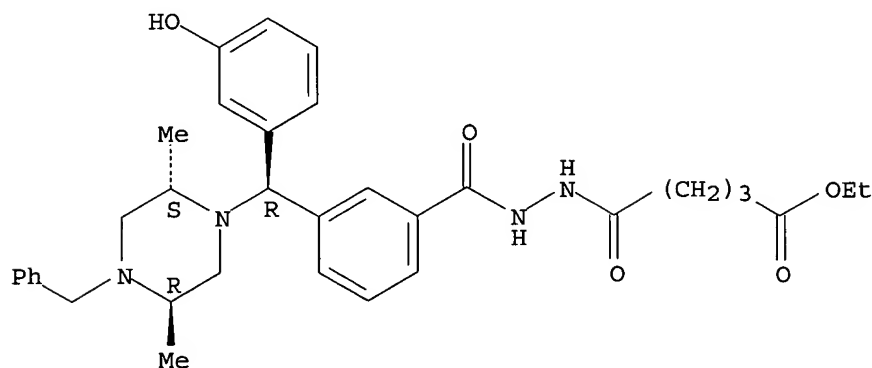
PAGE 1-B



RN 253801-27-3 HCAPLUS

CN Pentanedioic acid, monoethyl ester, 2-[3-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl] (3-hydroxyphenyl)methyl]benzoyl]hydrazide (9CI) (CA INDEX NAME)

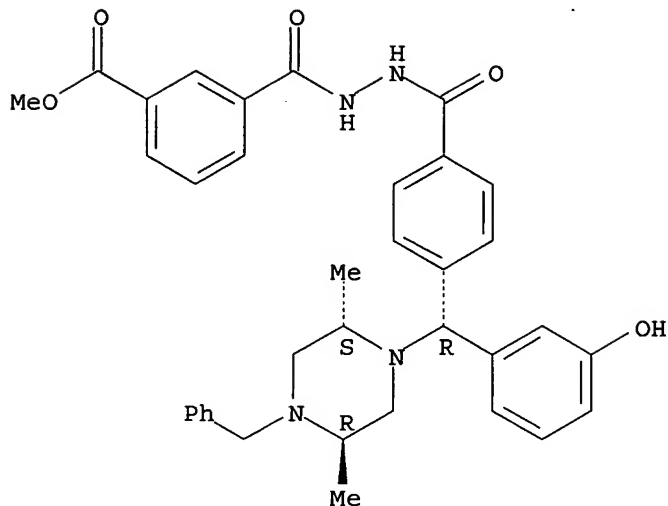
Absolute stereochemistry.



RN 253801-28-4 HCAPLUS

CN 1,3-Benzenedicarboxylic acid, monomethyl ester, 2-[4-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl] (3-hydroxyphenyl)methyl]benzoyl]hydrazide (9CI) (CA INDEX NAME)

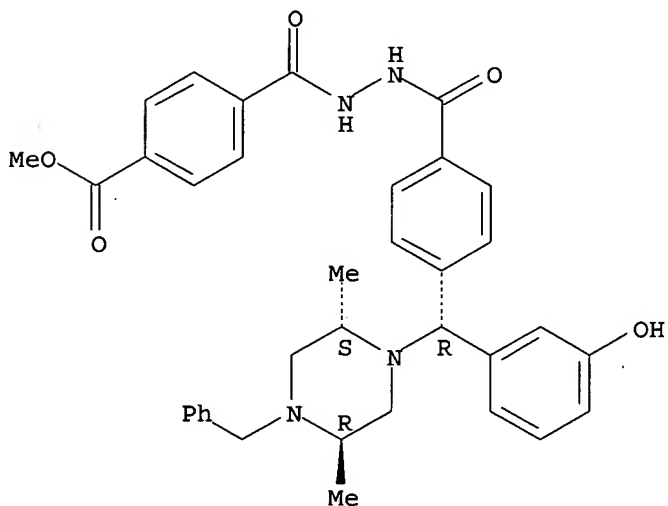
Absolute stereochemistry.



RN 253801-29-5 HCAPLUS

CN 1,4-Benzenedicarboxylic acid, monomethyl ester, 2-[4-[(R)-[(2S,5R)-2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl](3-hydroxyphenyl)methyl]benzoyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 24 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:811266 HCAPLUS

DOCUMENT NUMBER: 132:50253

TITLE: Preparation of tetrapeptides and their analogs that selectively bind mammalian opioid receptors

INVENTOR(S): Persons, Paul E.; Hauske, James; Hussoin, Roushan A.

PATENT ASSIGNEE(S): Sepracor, Inc., USA

SOURCE: PCT Int. Appl., 225 pp.

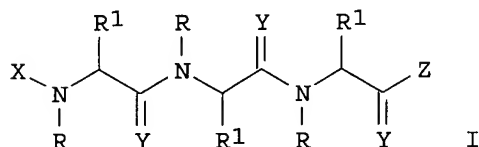
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965932	A1	19991223	WO 1999-US13638	19990618
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9945729	A1	20000105	AU 1999-45729	19990618
US 6548637	B1	20030415	US 1999-336314	19990618
PRIORITY APPLN. INFO.:			US 1998-89792P	P 19980618
			WO 1999-US13638	W 19990618
OTHER SOURCE(S):		MARPAT 132:50253		
GI				



AB Tetrapeptides or analogs or peptidomimetics thereof, e.g., I [X = COR, SO<sub>2</sub>R, CONR<sub>2</sub>; Y = O, S, NR, (H)<sub>2</sub>, (R)<sub>2</sub>; Z = R, OR, SR, NR<sub>2</sub>; R = H, Me, lower alkyl, lower heteroalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R<sub>1</sub> = H, Me, lower alkyl, alkyl, aryl, heteroaryl, side chain of any naturally occurring α-amino acids; R and R<sub>1</sub> taken together, when attached to adjacent N and C atoms, resp., may represent a ring with a total of 5-7 backbone atoms inclusive; said ring may contain two addnl. heteroatoms selected from O, S, N, Se and P; said ring may be unsubstituted or further substituted with one or more R, etc.], were prepared as ligands for mammalian opioid receptors. For example, N-[(2,5-difluorophenyl)amino]carbonyl]-Pro-Phe-HPA-NH<sub>2</sub> (II) (HPA = L-homophenylalanine) was synthesized from Rink resin-bound Fmoc-Pro-Phe-HPA and 2,5-difluorophenyl isocyanate; II demonstrated IC<sub>50</sub> < 1 μM and < 10 μM in μ- and κ-opioid receptor assays, resp. The title compds. comprise full agonists, partial agonists, and antagonists of mammalian opioid receptors.

IT 252767-19-4P 252767-24-1P 252767-36-5P  
252767-48-9P 252767-56-9P 252767-60-5P

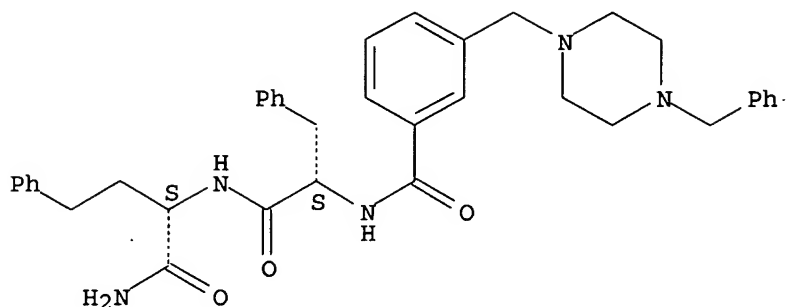
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of tetrapeptides and their analogs that selectively bind mammalian opioid receptors)

RN 252767-19-4 HCAPLUS

CN Benzenebutanamide, N-[3-[[4-(phenylmethyl)-1-piperazinyl]methyl]benzoyl]-L-phenylalanyl-α-amino-, (αS)- (9CI) (CA INDEX NAME)



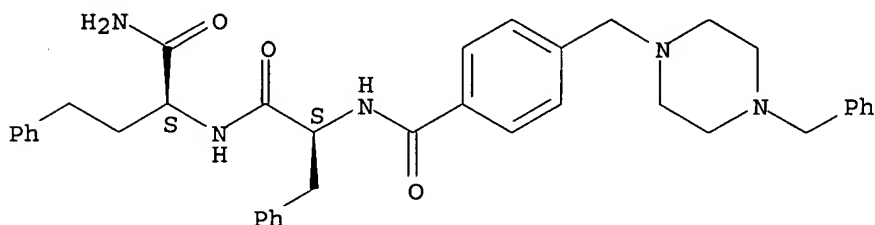
Absolute stereochemistry.



RN 252767-24-1 HCAPLUS

CN Benzenebutanamide, N-[4-[[4-(phenylmethyl)-1-piperazinyl]methyl]benzoyl]-L-phenylalanyl- $\alpha$ -amino-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

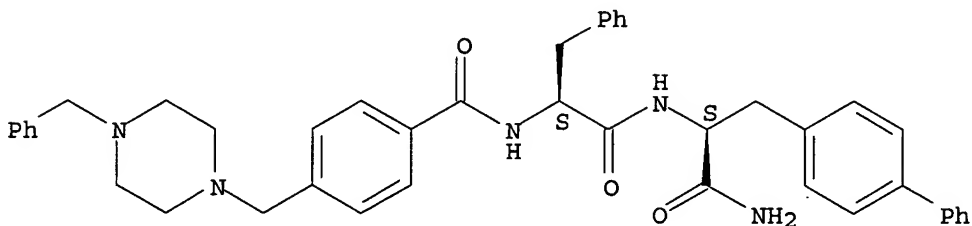
Absolute stereochemistry.



RN 252767-36-5 HCAPLUS

CN L-Alaninamide, N-[4-[[4-(phenylmethyl)-1-piperazinyl]methyl]benzoyl]-L-phenylalanyl-3-[1,1'-biphenyl]-4-yl- (9CI) (CA INDEX NAME)

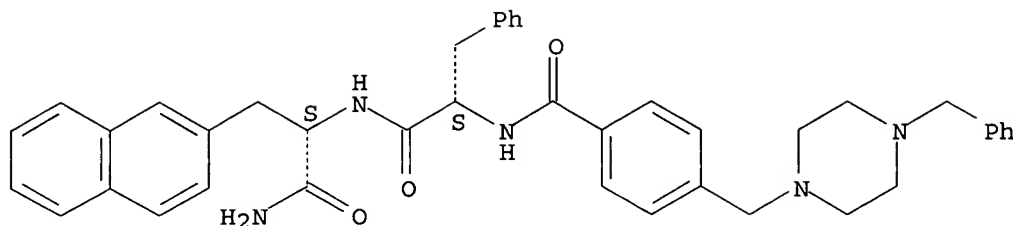
Absolute stereochemistry.



RN 252767-48-9 HCAPLUS

CN L-Alaninamide, N-[4-[[4-(phenylmethyl)-1-piperazinyl]methyl]benzoyl]-L-phenylalanyl-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

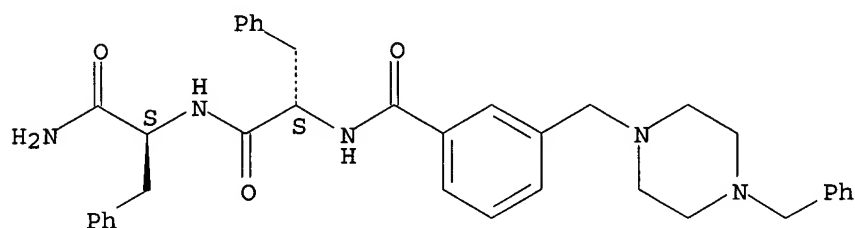
Absolute stereochemistry.



RN 252767-56-9 HCAPLUS

CN L-Phenylalaninamide, N-[3-[[4-(phenylmethyl)-1-piperazinyl]methyl]benzoyl]-L-phenylalanyl- (9CI) (CA INDEX NAME)

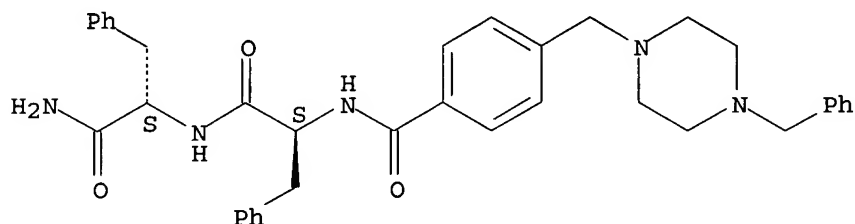
Absolute stereochemistry.



RN 252767-60-5 HCAPLUS

CN L-Phenylalaninamide, N-[4-[[4-(phenylmethyl)-1-piperazinyl]methyl]benzoyl]-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 25 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:691092 HCAPLUS

DOCUMENT NUMBER: 131:299287

TITLE: Preparation of N-(acylalkyl)benzamides as cysteine protease inhibitors

INVENTOR(S): Lubisch, Wilfried; Moller, Achim; Treiber, Hans-Jorg; Knopp, Monika

PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 104 pp.

CODEN: PIXXD2

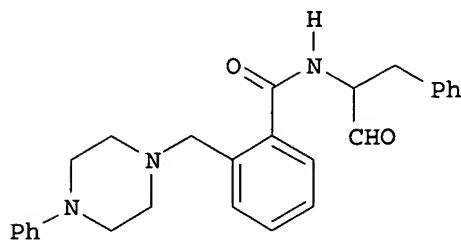
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954320	A1	19991028	WO 1999-EP2620	19990419
W: AL, AU, BG, BR, BY, CA, CN, CZ, GE, HR, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2328720	AA	19991028	CA 1999-2328720	19990419
AU 9938187	A1	19991108	AU 1999-38187	19990419
BR 9909819	A	20001219	BR 1999-9819	19990419
EP 1080083	A1	20010307	EP 1999-920705	19990419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
TR 200003071	T2	20010420	TR 2000-200003071	19990419
JP 2002512240	T2	20020423	JP 2000-544659	19990419
NO 2000005261	A	20001019	NO 2000-5261	20001019
BG 104885	A	20010531	BG 2000-104885	20001024
HR 2000000788	A1	20010630	HR 2000-788	20001117
ZA 2000006714	A	20011119	ZA 2000-6714	20001117
PRIORITY APPLN. INFO.:			DE 1998-19817460	A 19980420
OTHER SOURCE(S):			WO 1999-EP2620	W 19990419
GI			MARPAT 131:299287	

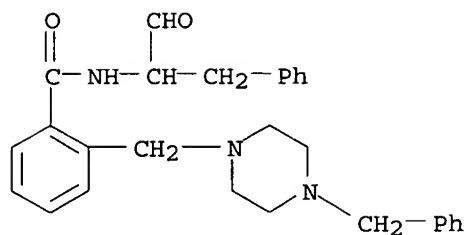


AB R1Z1[Z2(Z3R3)]CONHCHR4COR5 [R1 = H, alkyl, (hetero)aryl; R3 = (di)[(phenyl)alkyl]amino, pyrrolidino, piperidino, etc.; R4 = [(hetero)aryl]alkyl; R5 = H, CO2R11, COR; R = (un)substituted pyrrolidino, -piperidino, -piperazino; R11 = H, (phenyl)alkyl, etc.; Z1 = bond, alkylene, O, CO, etc.; Z2 = (un)substituted phenylene, -pyridinediyl, -imidazolediyl, etc.; Z3 = (CH2)1-3] were prepared as cysteine protease inhibitors (no data). Thus, 2-(ClH2C)C6H4CO2Me was aminated by 1-phenylpiperazine and the saponified product amidated by PhCH2CH(NH2)CH2OH to give, after oxidation, title compound I.

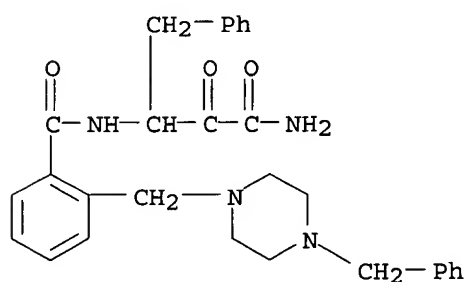
IT 247061-66-1P 247061-67-2P 247061-70-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of N-(acylalkyl)benzamides as cysteine protease inhibitors)

RN 247061-66-1 HCAPLUS

CN Benzamide, N-(1-formyl-2-phenylethyl)-2-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



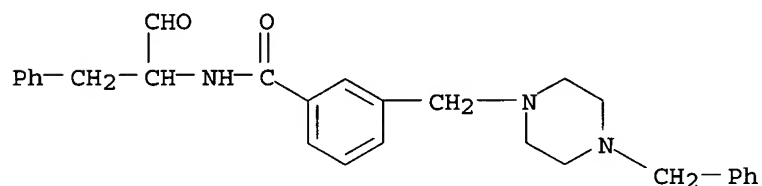
RN 247061-67-2 HCAPLUS  
 CN Benzenebutanamide,  $\alpha$ -oxo- $\beta$ -[[2-[[4-(phenylmethyl)-1-piperazinyl]methyl]benzoyl]amino]- (9CI) (CA INDEX NAME)



RN 247061-70-7 HCAPLUS  
 CN Benzamide, N-(1-formyl-2-phenylethyl)-3-[[4-(phenylmethyl)-1-piperazinyl]methyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

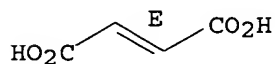
CRN 247061-69-4  
 CMF C28 H31 N3 O2



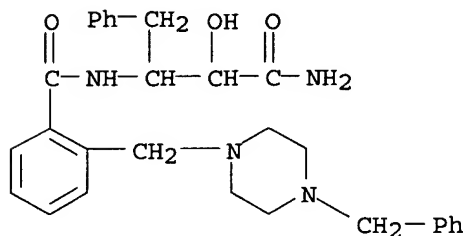
CM 2

CRN 110-17-8  
 CMF C4 H4 O4

Double bond geometry as shown.



IT 247061-97-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of N-(acylalkyl)benzamides as cysteine protease inhibitors)  
 RN 247061-97-8 HCAPLUS  
 CN Benzenebutanamide,  $\alpha$ -hydroxy- $\beta$ -[[2-[[4-(phenylmethyl)-1-  
 piperazinyl]methyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

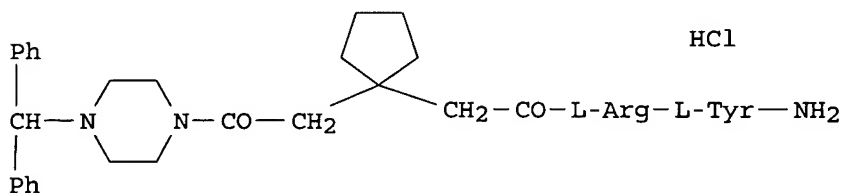


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 26 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1999:684275 HCAPLUS  
 DOCUMENT NUMBER: 131:286823  
 TITLE: Preparation of novel peptides for use as NPY  
 antagonists  
 INVENTOR(S): Esser, Franz; Schnorrenberg, Gerd; Dollinger, Horst;  
 Gaida, Wolfram  
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany  
 SOURCE: Ger. Offen., 44 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19816932	A1	19991021	DE 1998-19816932	19980416
PRIORITY APPLN. INFO.:			DE 1998-19816932	19980416
OTHER SOURCE(S):	MARPAT	131:286823		

GI



I

AB Title compds. of the formula  $RR_1NC(O)-A-C(O)-B-D-NH_2$ , where R,  $R_1$   
 independently = H, (un)substituted alkyl, substituted Ph, pyrrolidinyl,  
 morpholino, perhydroazepinyl, amino, alkylamino, or (un)substituted

1,2,3,4-tetrahydro-pyrimido[1,2-a]benzimidazole, A = (un)substituted (un)saturated alicyclic, (un)substituted alkyl, or CH<sub>2</sub>-X-CH<sub>2</sub>, where X = O, S, or substituted N, and B and D = (un)substituted D- or L-amino acid residues, were prepared for pharmaceutical use as NPY antagonists in the treatment of cardiovascular disturbances, coronary, cerebral, or renal vasospasm, obesity, bulimia, or asthma. Thus, 1-(diphenyl-methyl)-piperazine was reacted with 3,3-tetramethylene-glutaric anhydride and the product condensed with a dipeptide (preparation given) to give I in 41% yield. In in vitro receptor affinity tests using NPY receptor preps. from rabbits, I had IC<sub>50</sub> 4.0x10<sup>-8</sup> M.

IT 246161-72-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of for use as NPY antagonists)

RN 246161-72-8 HCAPLUS

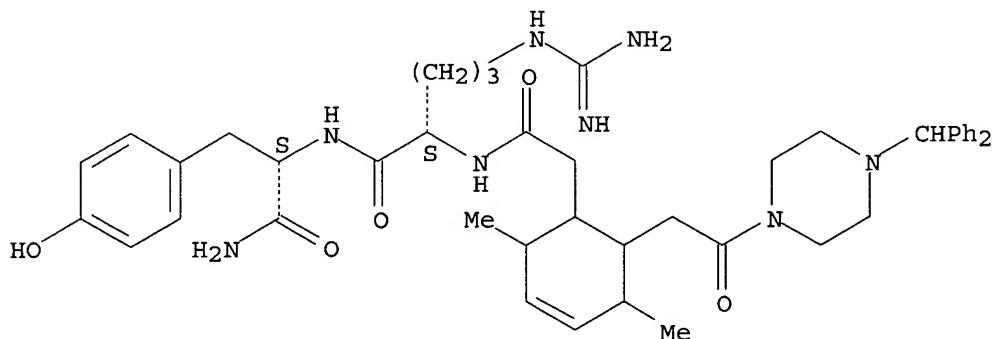
CN L-Tyrosinamide, N2-[[6-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethyl]-2,5-dimethyl-3-cyclohexen-1-yl]acetyl]-L-arginyl-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 246161-71-7

CMF C44 H58 N8 O5

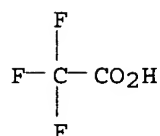
Absolute stereochemistry.



CM 2

CRN 76-05-1

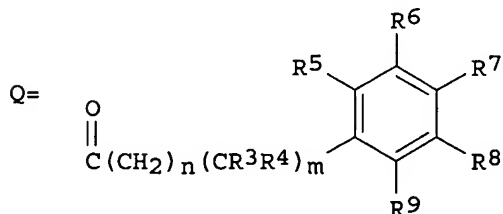
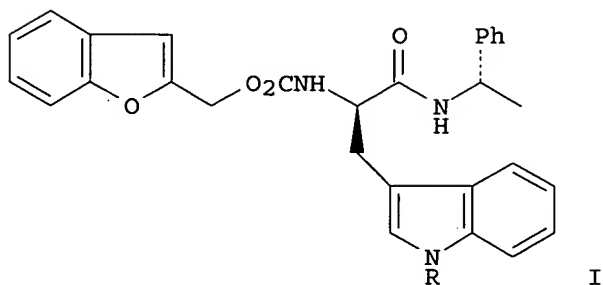
CMF C2 H F3 O2



L12 ANSWER 27 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1999:672811 HCAPLUS  
DOCUMENT NUMBER: 131:299365

TITLE: Preparation of prodrugs of benzofuranylmethyl carbamate NK1 antagonists  
 INVENTOR(S): Chan, Oilun Helen; Chen, Michael Huai Gu; Goel, Om Prakash; Hershenson, Fred M.; Zhu, Zhijian  
 PATENT ASSIGNEE(S): Warner-Lambert Company, USA  
 SOURCE: PCT Int. Appl., 54 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952903	A1	19991021	WO 1999-US6041	19990319
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2323047	AA	19991021	CA 1999-2323047	19990319
CA 2323047	C	20050315		
AU 9930114	A1	19991101	AU 1999-30114	19990319
EP 1075472	A1	20010214	EP 1999-911477	19990319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002511467	T2	20020416	JP 2000-543460	19990319
US 6258800	B1	20010710	US 2000-601570	20000803
PRIORITY APPLN. INFO.:			US 1998-81881P	P 19980415
			WO 1999-US6041	W 19990319
OTHER SOURCE(S):		MARPAT 131:299365		
GI				



AB Aqueous soluble prodrugs I [R = CH<sub>2</sub>OZ, C(O)OCH<sub>2</sub>OZ, Z, wherein Z = Q, P(O)(OH)<sub>2</sub>, C(O)Q<sub>1</sub>; n = 0-3; m = 0, 1] of certain tachykinin antagonists (NK1 antagonists) useful in the treatment of emesis, were prepared E.g., {3-[2-(benzofuran-2-ylmethoxycarbonylamino)-2-(1-phenylethylcarbamoyl)propyl]indol-1-yl}phosphonic acid disodium salt was prepared

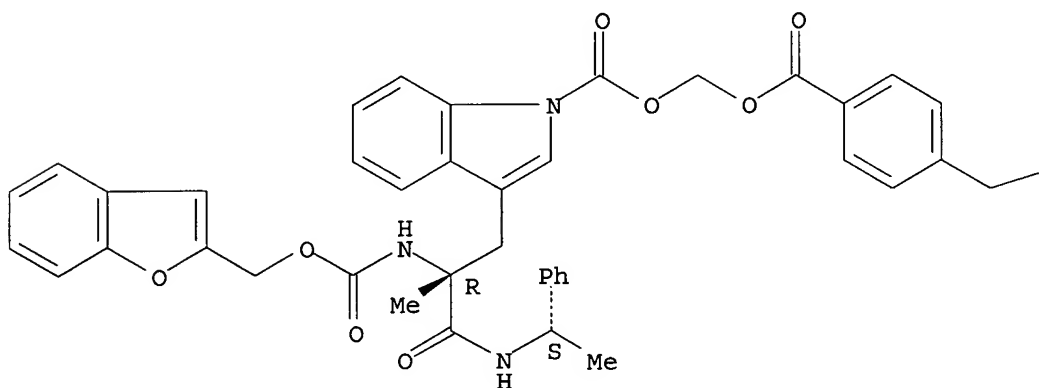
IT **247018-24-2P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of prodrugs of benzofuranylmethyl carbamate NK1 antagonists)

RN 247018-24-2 HCAPLUS

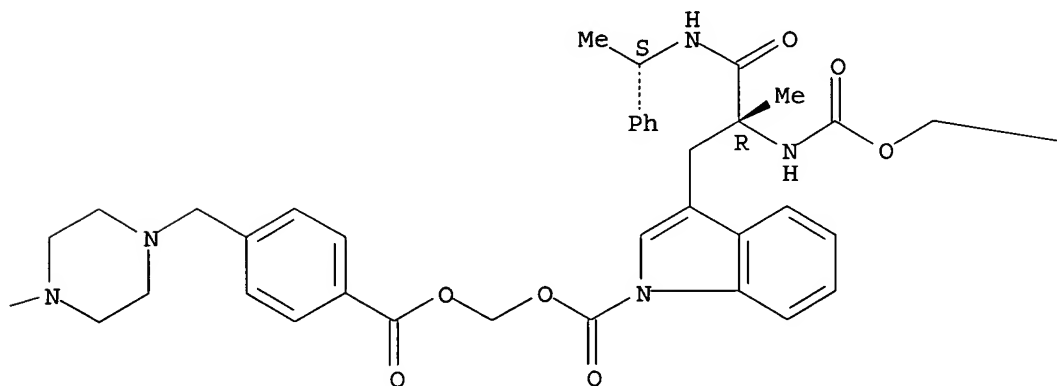
CN 1H-Indole-1-carboxylic acid, 3-[(2R)-2-[[[(2-benzofuranylmethoxy)carbonyl]amino]-2-methyl-3-oxo-3-[[[(1S)-1-phenylethyl]amino]propyl]-, 1,4-piperazinediylbis(methylene-4,1-phenylenecarbonyloxymethylene) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

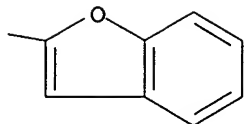


PAGE 1-B





PAGE 1-C



IT 247018-16-2P

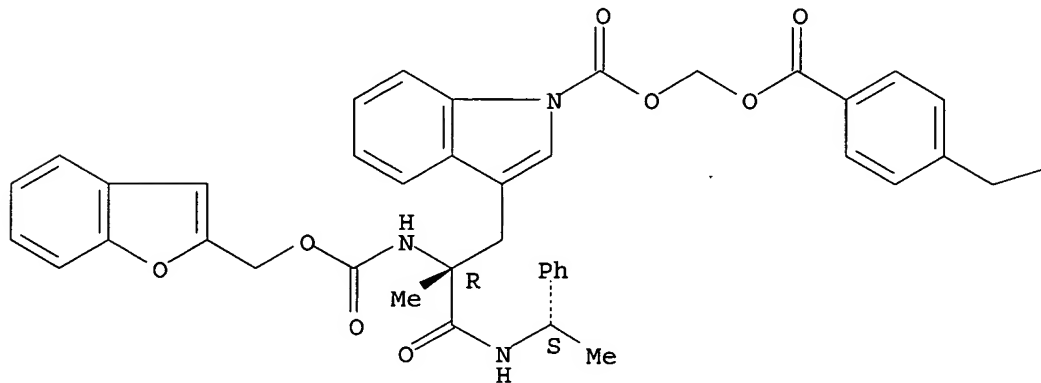
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of prodrugs of benzofuranylmethyl carbamate NK1 antagonists)

RN 247018-16-2 HCAPLUS

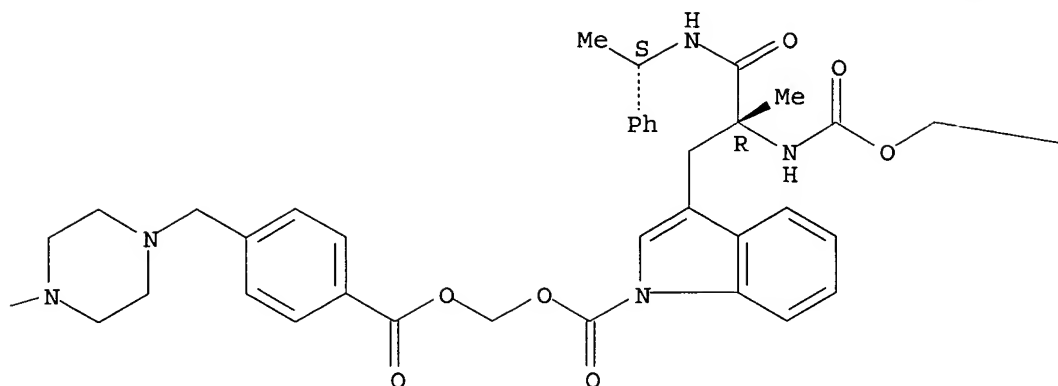
CN 1H-Indole-1-carboxylic acid, 3-[(2R)-2-[[[(2-benzofuranylmethoxy)carbonyl]amino]-2-methyl-3-oxo-3-[[[(1S)-1-phenylethyl]amino]propyl]-, 1,4-piperazinediylbis(methylene-4,1-phenylenecarbonyloxymethylene) ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

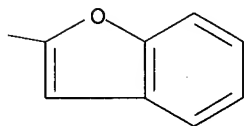
PAGE 1-A



PAGE 1-B



PAGE 1-C



● 2 HCl

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 28 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:249093 HCAPLUS

DOCUMENT NUMBER: 130:312099

TITLE: Preparation of peptide-containing  $\alpha$ -ketoamide cysteine and serine protease inhibitors

INVENTOR(S): Chatterjee, Sankar; Mallamo, John P.; Bihovsky, Ron; Wells, Gregory J.

PATENT ASSIGNEE(S): Cephalon Inc., USA

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

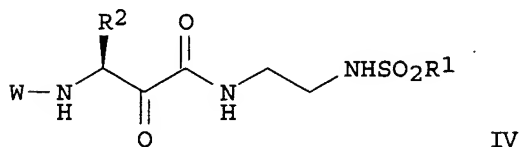
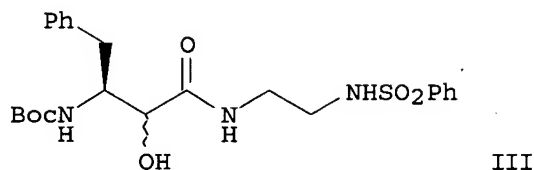
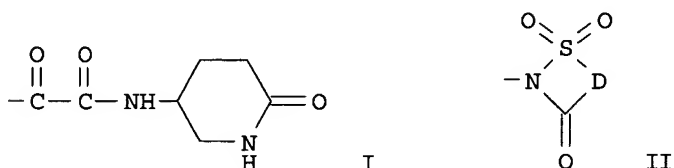
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917790	A1	19990415	WO 1998-US21055	19981007
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

US 6150378	A	20001121	US 1998-166808	19981006
CA 2304116	AA	19990415	CA 1998-2304116	19981007
AU 9910686	A1	19990427	AU 1999-10686	19981007
AU 749555	B2	20020627		
EP 1021199	A1	20000726	EP 1998-953275	19981007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001518513	T2	20011016	JP 2000-514661	19981007
NZ 503550	A	20020201	NZ 1998-503550	19981007
US 6288231	B1	20010911	US 2000-527540	20000316
MX 200003419	A	20001113	MX 2000-3419	20000407
US 2002055616	A1	20020509	US 2001-879336	20010612
US 6703368	B2	20040309		
US 2004102609	A1	20040527	US 2003-685923	20031014
PRIORITY APPLN. INFO.:			US 1997-61309P	P 19971007
			US 1998-166808	A 19981006
			WO 1998-US21055	W 19981007
			US 2000-527540	A3 20000316
			US 2001-879336	A3 20010612
OTHER SOURCE(S):			MARPAT 130:312099	
GI				



AB Title compds. of formula Q-(Aaa)n-(NR<sub>3</sub>-CH(R<sub>1</sub>)-CO)<sub>q</sub>-NH-CH(R<sub>2</sub>)-Z [Q = G-B-(CHR<sub>4</sub>)<sub>v</sub>; R<sub>4</sub> = H, C1-4 alkyl; v = 0-2; B = CO, OC(O), S(O)<sub>m</sub>, CH<sub>2</sub>, bond, NR<sub>5</sub>CO, S(O)<sub>m</sub>-A-CO, CO-A-CO; R<sub>5</sub> = H, alkyl; m = 0-2; A = (un)substituted alkylene or cycloalkylene; G = H, a blocking group, alkenyl, (un)substituted alkyl, aryl, heterocyclyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, or arylheteroalkyl; Aaa = an amino acid optionally containing blocking groups; n = 0-3; R<sub>1</sub> and R<sub>2</sub> = independently H, heteroaryl, (un)substituted alkyl, arylalkyl, heteroalkyl, heteroarylalkyl, or alkoxyalkyl, (un)substituted naturally occurring amino acid side chain; R<sub>3</sub>

= H, alkyl, arylalkyl, heteroalkyl, heteroarylalkyl, alkoxyalkyl, (un)substituted naturally occurring amino acid side chain, blocking group, etc.; q = 0-1; Z = CO-CO-NH-X-A1-K or I; X = bond, O; A1 = A; K = N(R10)Y, II, SO2N(R8)(R10); D = fused aryl, or heteroaryl group; R11 = alkoxy, aryloxy, NHR12; R9, R12 = H, (un)substituted alkyl, aryl, or heteroaryl; Y = SO2R8, CONHR9, CSNHR9, C(=NCN)R11, C(=NCONHR10)R11, CO2R8; R8 = (un)substituted alkyl, alkoxy, aryl, or heterocyclyl; R10 = H, alkyl; R8 and R10 may combine with the N atom to which they are attached to form an N-containing heterocyclic ring; R9 may be combined with an A1 alkylene group to form an N-containing heterocyclic ring] or their pharmaceutically acceptable salts, were prepared as cysteine and serine protease inhibitors. Thus, III (preparation given) was oxidized by Dess-Martin periodinane, deprotected, and coupled with PhSO2-L-Pro-OH to yield compound IV (W = PhSO2-L-Pro, R2 = PhCH2, R1 = Ph) which exhibited 78% inhibition of calpain I at 10  $\mu$ M. Compound IV (W = MeSO2-D-Ser(CH2Ph), R2 = CH2OMe, R1 = Ph) exhibited 100% inhibition of calpain I at 10  $\mu$ M. Methods for the use of the protease inhibitors are also described.

IT 223513-84-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

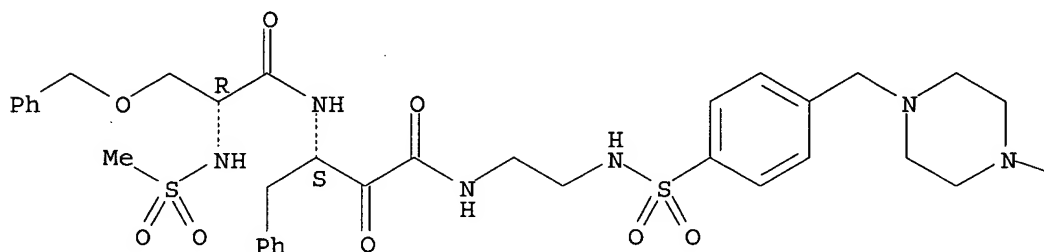
(preparation of peptide-containing  $\alpha$ -ketoamide cysteine and serine protease inhibitors)

RN 223513-84-6 HCAPLUS

CN Benzenebutanamide,  $\beta$ -[[[(2R)-2-[(methylsulfonyl)amino]-1-oxo-3-(phenylmethoxy)propyl]amino]- $\alpha$ -oxo-N-[2-[[[4-[[4-(phenylmethyl)-1-piperazinyl]methyl]phenyl]sulfonyl]amino]ethyl]-, ( $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 29 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:70873 HCAPLUS  
 DOCUMENT NUMBER: 130:223667  
 TITLE: Synthesis of Ordered Polymer by Direct Polycondensation. 9. Ordered Poly(amide-acylhydrazide-amide) from Three Nonsymmetric Monomers  
 AUTHOR(S): Yu, Shuyan; Seino, Hiroshi; Ueda, Mitsuru  
 CORPORATE SOURCE: Department of Human Sensing and Functional Sensor Engineering Graduate School of Engineering, Yamagata University, Yonezawa Yamagata, 992-8510, Japan  
 SOURCE: Macromolecules (1999), 32(4), 1027-1035  
 CODEN: MAMOBX; ISSN: 0024-9297  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB An ordered (-ccfebadabef-) poly(amide-acylhydrazide-amide) was prepared by the direct polycondensation of 5-(3-carboxypropyl)-2-isopropoxybenzoic acid (XabX), bis(4-nitrophenyl) isophthalate (XccX), piperazine (YddY), and 4-aminobenzohydrazide (YefY), using the condensing agent diphenyl(2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate (I). The polymerization was carried out by mixing the dicarboxylic acid, diester, condensing agent I, and triethylamine (TEA) in N-methyl-2-pyrrolidinone (NMP) for 3 h at room temperature, followed by addition of piperazine and aminobenzohydrazide at -15°. The mixture was stirred at -15° for 2 h, room temperature for 24 h, and 70° for 4 d in the presence of 1-hydroxybenzotriazole (HOBT). The resulting polymer has inherent viscosity of 0.20 dL/g in NMP, measured at a concentration of 0.5 g/dL at 30°. The feasibility of formation of the ordered polymer from three nonsym. monomers was demonstrated by studying the model reactions in detail. The authentic ordered and random polymers were prepared to verify the structure of the ordered polymer. The microstructure of the polymers obtained was studied by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy; the polymer obtained by direct polycondensation has the expected ordered structure.

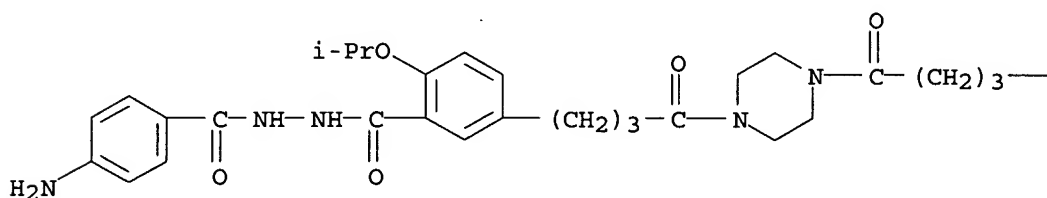
IT 221041-42-5P, 5,5'-[3,3'-(Piperazine-1,4-dicarbonyl)dipropylene]bis[N'-(4-aminobenzoyl)-2-isopropoxybenzohydrazide]  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate in step polyamide preparation; preparation of authentic ordered poly(amide-acylhydrazide-amide) via sequential steps using condensing reagent)

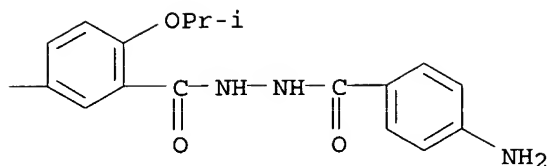
RN 221041-42-5 HCAPLUS

CN Benzoic acid, 3,3'-[1,4-piperazinediylbis(4-oxo-4,1-butanediyl)]bis[6-(1-methylethoxy)-, bis[2-(4-aminobenzoyl)hydrazide] (9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 30 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:7977 HCAPLUS

DOCUMENT NUMBER: 130:66509

TITLE: Preparation of N-benzylpiperazines as antiinflammatory agents

INVENTOR(S): Bauman, John G.; Buckman, Brad O.; Ghannam, Ameen F.; Hesselgesser, Joseph E.; Horuk, Richard; Islam, Imadul; Liang, Meina; May, Karen B.; Monahan, Sean D.; Morissey, Michael M.; Ng, Howard P.; Wei, Guo Ping; Xu, Wei; Zheng, Wei

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 309 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

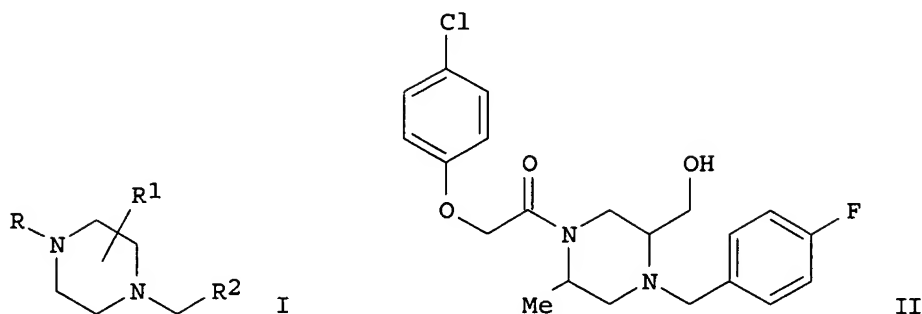
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856771	A2	19981217	WO 1998-EP3503	19980611
WO 9856771	A3	19990311		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2293382	AA	19981217	CA 1998-2293382	19980611
AU 9886258	A1	19981230	AU 1998-86258	19980611
AU 735462	B2	20010712		
EP 988292	A2	20000329	EP 1998-937467	19980611
EP 988292	B1	20030212		
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EE 9900565	A	20000615	EE 1999-565	19980611
EE 4056	B1	20030616		
JP 2002503239	T2	20020129	JP 1999-501611	19980611
AT 232522	E	20030215	AT 1998-937467	19980611
EE 200200682	A	20030415	EE 2002-200200682	19980611
EE 200200683	A	20030415	EE 2002-200200683	19980611
EE 200200684	A	20030415	EE 2002-200200684	19980611
IL 132398	A1	20040831	IL 1998-132398	19980611
NO 9906068	A	20000211	NO 1999-6068	19991209

MX 9911506	A	20000430	MX 1999-11506	19991210
NO 2003001373	A	20000211	NO 2003-1373	20030326
PRIORITY APPLN. INFO.:			US 1997-873599	A 19970612
			US 1998-94397	A 19980609
			WO 1998-EP3503	W 19980611

OTHER SOURCE(S): MARPAT 130:66509  
GI



AB Title compds. [I; R = R<sub>3</sub>Z<sub>3</sub>Z<sub>2</sub>Z<sub>1</sub>; R<sub>1</sub> = ≥1 of halo, alkyl, aryl, etc.; R<sub>2</sub> = (un)substituted Ph; R<sub>3</sub> = (un)substituted carbocyclic ring system (sic) or (un)substituted heterocyclic ring system (sic); Z<sub>1</sub> = bond, CH<sub>2</sub>, CO, etc.; Z<sub>2</sub> = alkylene or alkylidene; Z<sub>3</sub> = bind, O, CH<sub>2</sub>, (alkyl)imino, etc.] were prepared as chemokine inhibitors (no data). Thus, (2R,5S)-1-(4-fluorobenzyl)-2-hydroxymethyl-5-methylpiperazine was N-acylated by 4-ClC<sub>6</sub>H<sub>4</sub>OCH<sub>2</sub>COCl to give title compound (R,R)-II.

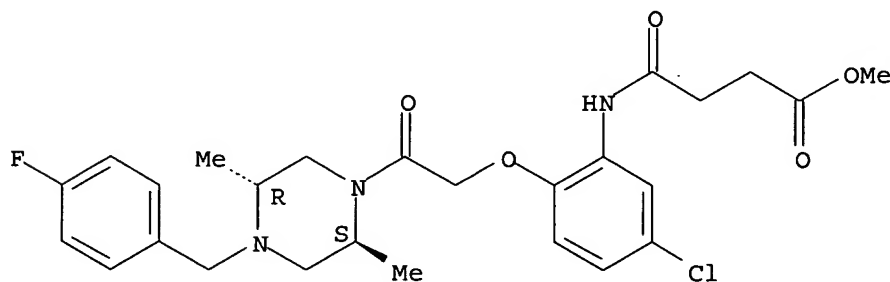
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217645-12-0P 217645-13-1P 217645-14-2P  
217645-15-3P 217645-16-4P 217645-17-5P  
217645-18-6P 217645-19-7P 217645-20-0P  
217645-21-1P 217645-22-2P 217645-23-3P  
217645-25-5P 217645-29-9P 217646-95-2P  
217646-96-3P 217647-07-9P 217647-39-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-benzylpiperazines as antiinflammatory agents)

RN 217644-74-1 HCAPLUS

CN Butanoic acid, 4-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-4-oxo-, methyl ester, rel- (9CI) (CA INDEX NAME)

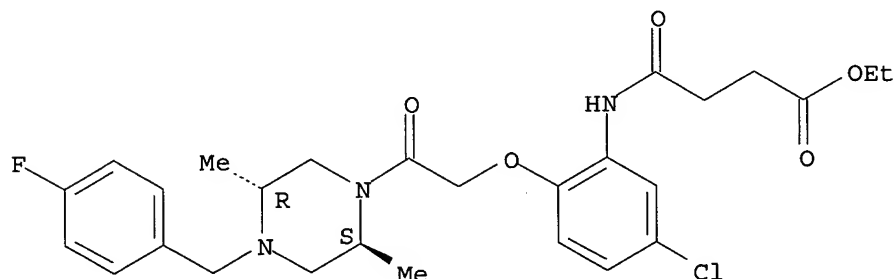
Relative stereochemistry.



RN 217644-75-2 HCAPLUS

CN Butanoic acid, 4-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-4-oxo-, ethyl ester, rel- (9CI) (CA INDEX NAME)

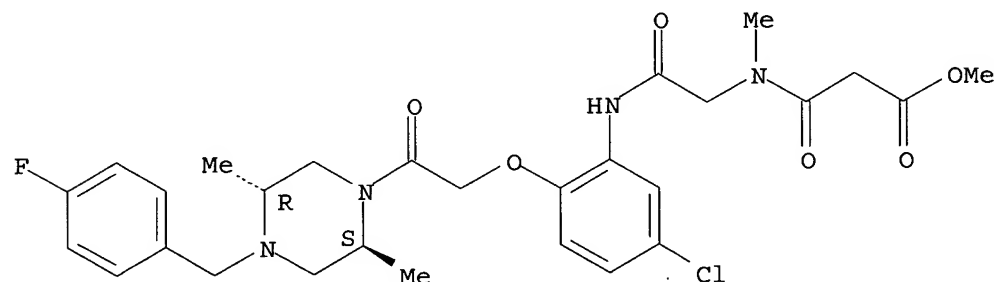
Relative stereochemistry.



RN 217645-11-9 HCAPLUS

CN Propanoic acid, 3-[[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]methylamino]-3-oxo-, methyl ester, rel- (9CI) (CA INDEX NAME)

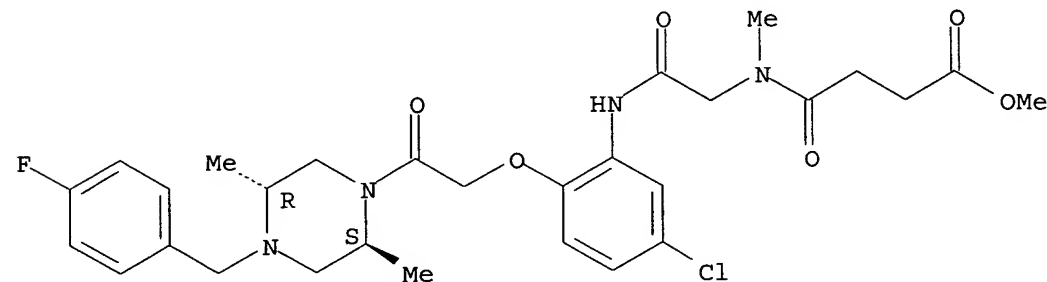
Relative stereochemistry.



RN 217645-12-0 HCAPLUS

CN Butanoic acid, 4-[[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]methylamino]-4-oxo-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 217645-13-1 HCAPLUS

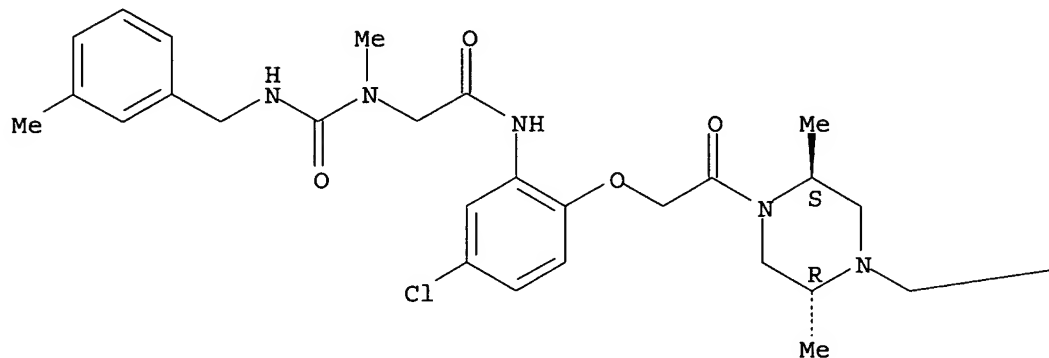
CN Acetamide, N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-



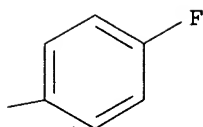
dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-2-[methyl[[[(3-methylphenyl)methyl]amino]carbonyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



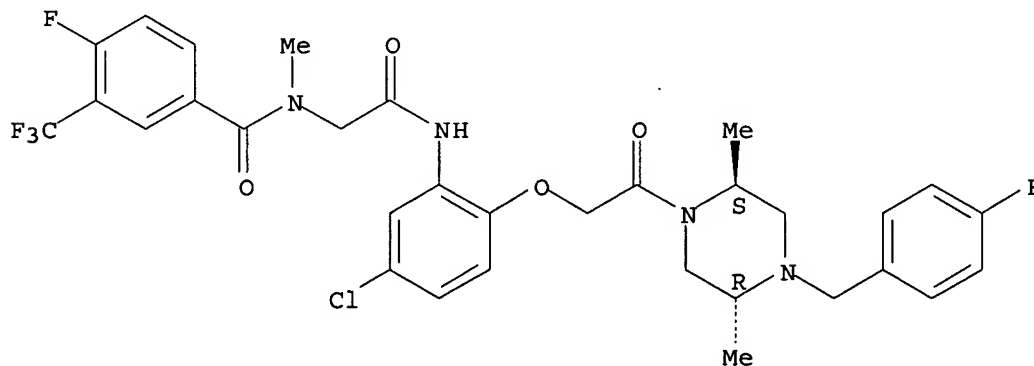
PAGE 1-B



RN 217645-14-2 HCAPLUS

CN Benzamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-4-fluoro-N-methyl-3-(trifluoromethyl)-, rel- (9CI) (CA INDEX NAME)

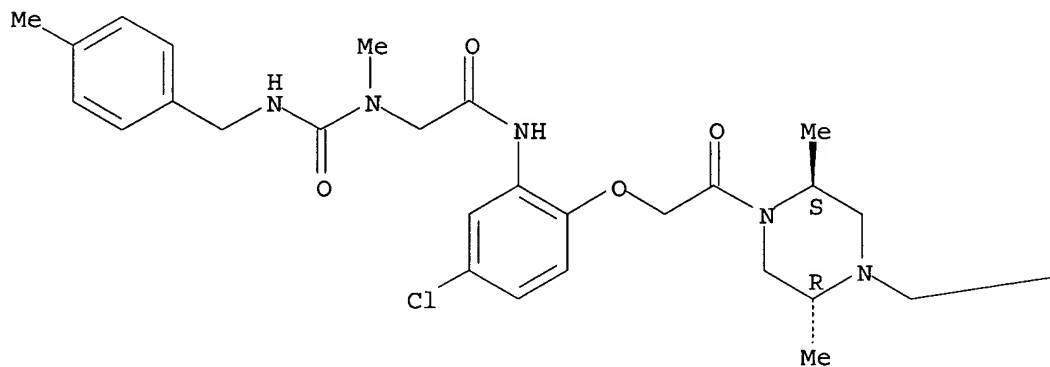
Relative stereochemistry.



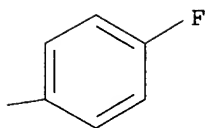
RN 217645-15-3 HCAPLUS  
 CN Acetamide, N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-2-[methyl[[[(4-methylphenyl)methyl]amino]carbonyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

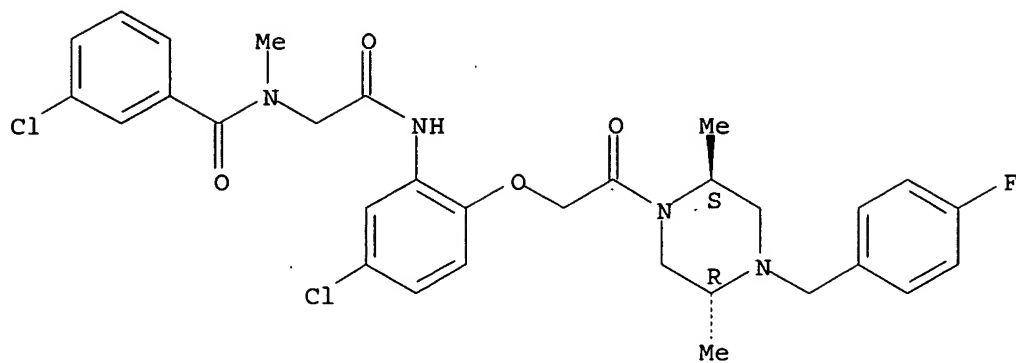


PAGE 1-B



RN 217645-16-4 HCAPLUS  
 CN Benzamide, 3-chloro-N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-N-methyl-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

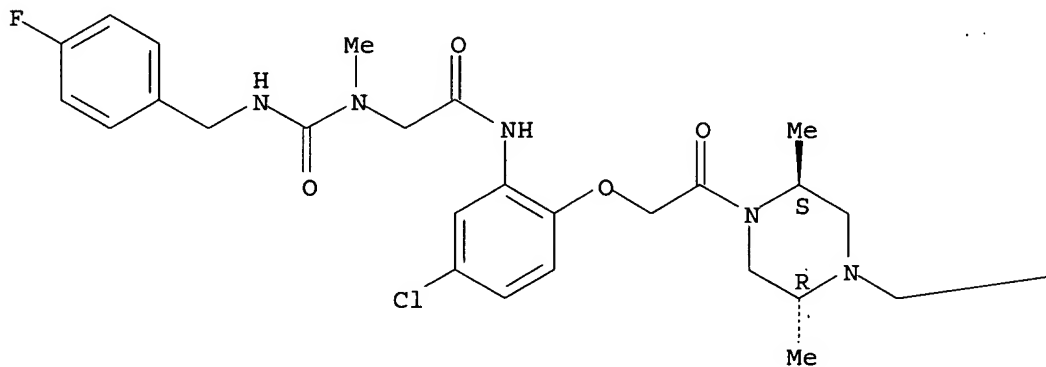


RN 217645-17-5 HCAPLUS

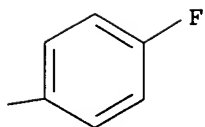
CN Acetamide, N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-2-[[[(4-fluorophenyl)methyl]amino]carbonyl]methylamino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



PAGE 1-B

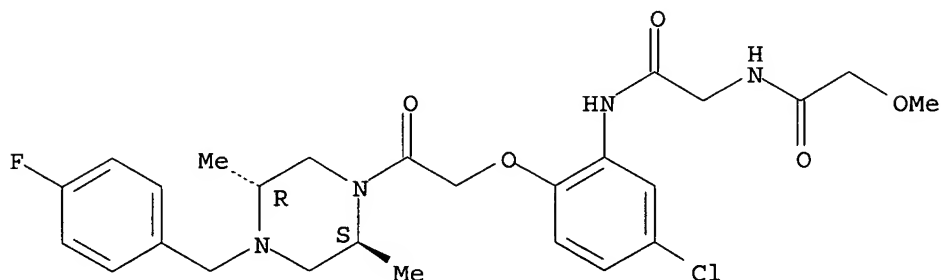


RN 217645-18-6 HCAPLUS

CN Acetamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-

dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-2-methoxy-,  
rel- (9CI) (CA INDEX NAME)

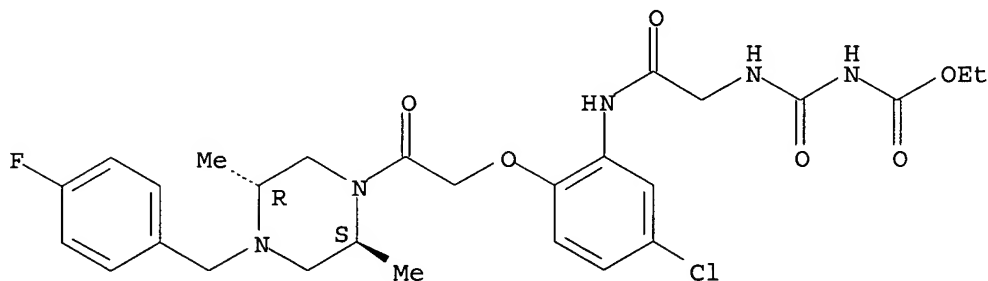
Relative stereochemistry.



RN 217645-19-7 HCAPLUS

CN Carbamic acid, [[[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]amino]carbonyl]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

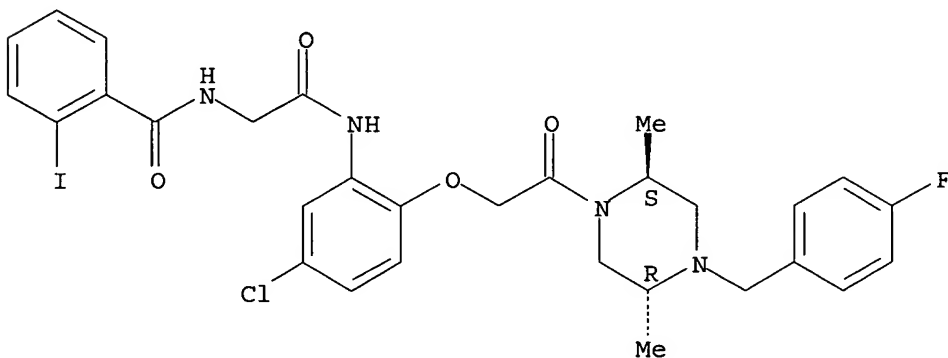
Relative stereochemistry.



RN 217645-20-0 HCAPLUS

CN Benzamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-2-iodo-, rel- (9CI) (CA INDEX NAME)

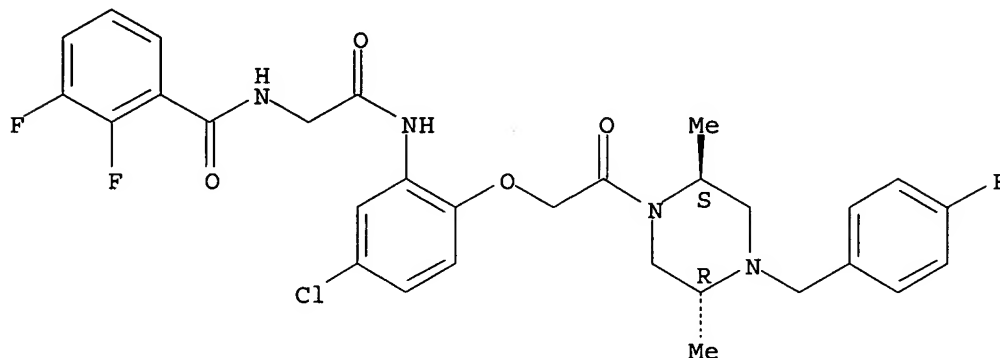
Relative stereochemistry.



RN 217645-21-1 HCAPLUS

CN Benzamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-2,3-difluoro-, rel- (9CI) (CA INDEX NAME)

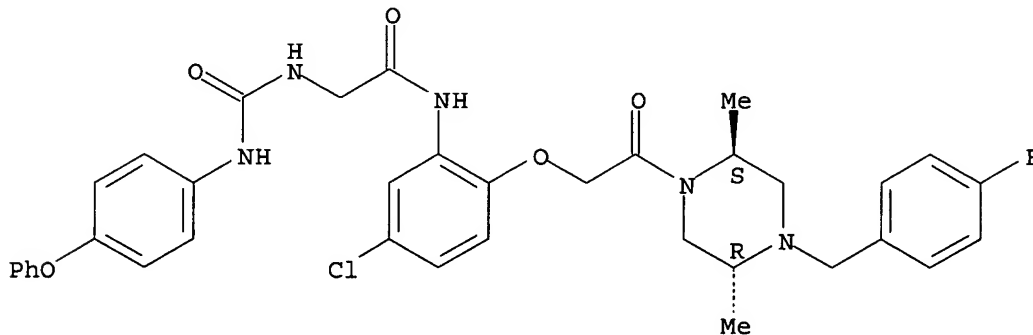
Relative stereochemistry.



RN 217645-22-2 HCAPLUS

CN Acetamide, N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-2-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-, rel- (9CI) (CA INDEX NAME)

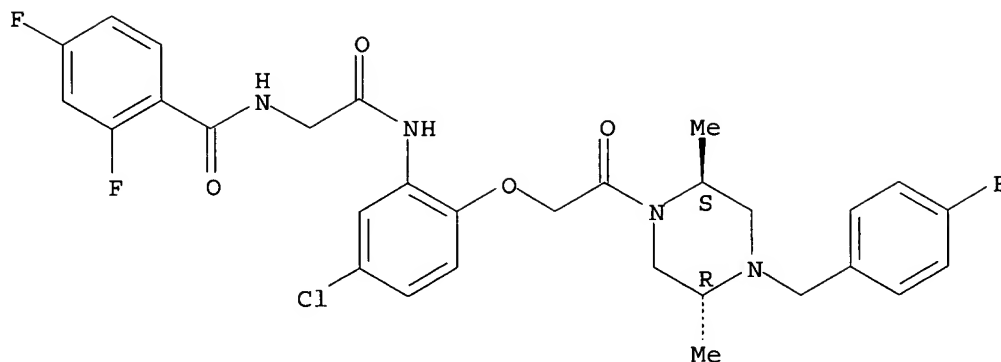
Relative stereochemistry.



RN 217645-23-3 HCAPLUS

CN Benzamide, N-[2-[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]-2-oxoethyl]-2,4-difluoro-, rel- (9CI) (CA INDEX NAME)

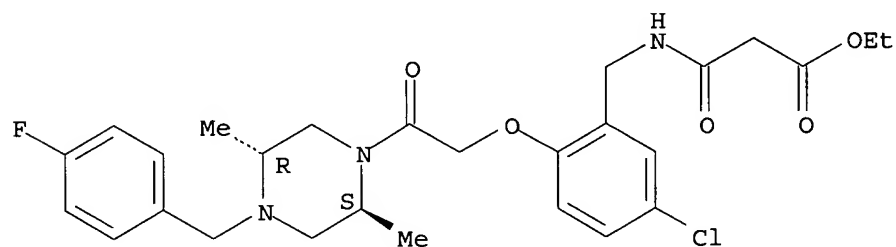
Relative stereochemistry.



RN 217645-25-5 HCAPLUS

CN Propanoic acid, 3-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]amino]-3-oxo-, ethyl ester, rel- (9CI) (CA INDEX NAME)

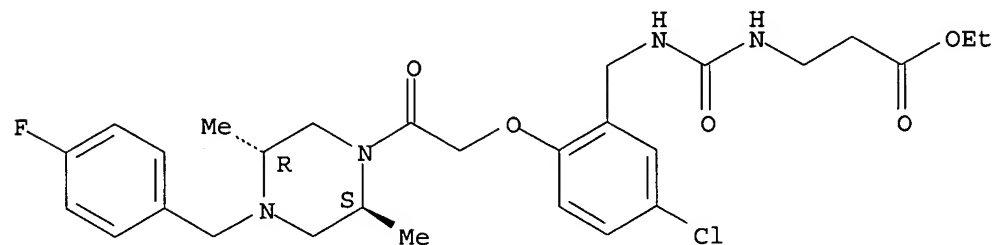
Relative stereochemistry.



RN 217645-29-9 HCAPLUS

CN  $\beta$ -Alanine, N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]methyl]amino]carbonyl]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

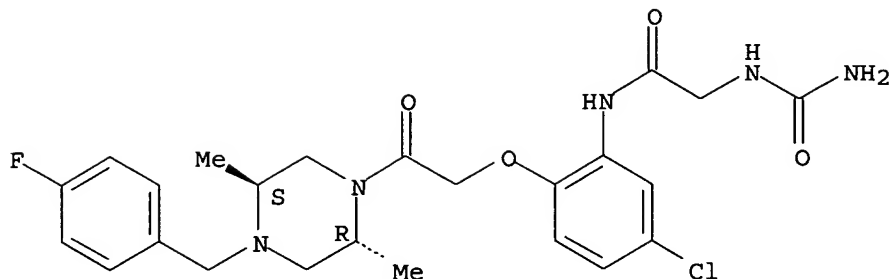
Relative stereochemistry.



RN 217646-95-2 HCAPLUS

CN Acetamide, 2-[(aminocarbonyl)amino]-N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-, rel- (9CI) (CA INDEX NAME)

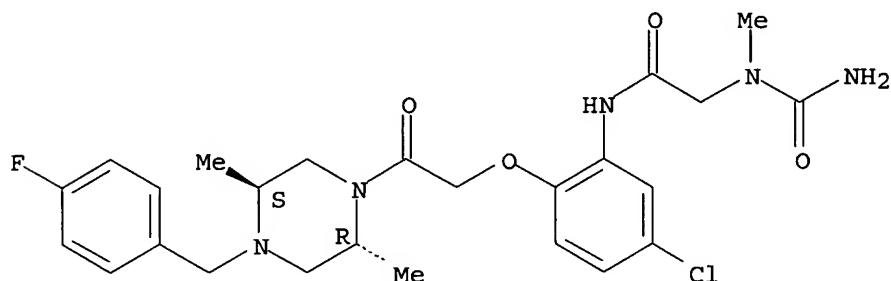
Relative stereochemistry.



RN 217646-96-3 HCAPLUS

CN Acetamide, 2-[(aminocarbonyl)methylamino]-N-[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]-, rel- (9CI) (CA INDEX NAME)

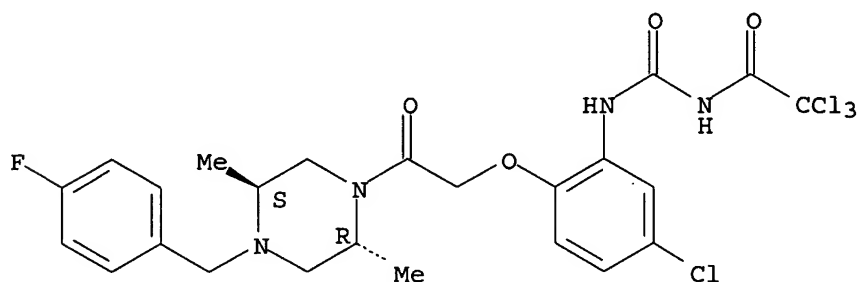
Relative stereochemistry.



RN 217647-07-9 HCAPLUS

CN Acetamide, 2,2,2-trichloro-N-[[[5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]phenyl]amino]carbonyl]-, rel- (9CI) (CA INDEX NAME)

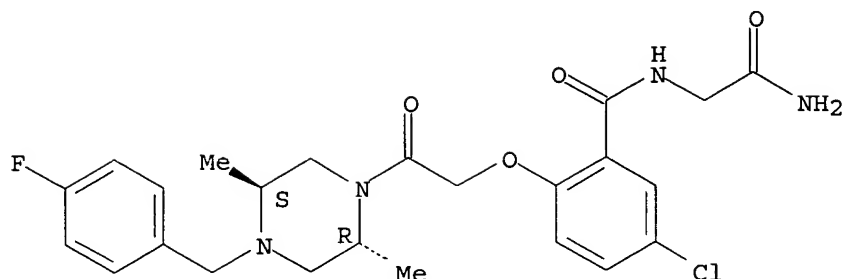
Relative stereochemistry.



RN 217647-39-7 HCAPLUS

CN Benzamide, N-(2-amino-2-oxoethyl)-5-chloro-2-[2-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 31 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:744941 HCAPLUS

DOCUMENT NUMBER: 130:14261

TITLE: Preparation of methionine derivatives as inhibitors of protein isoprenyl transferases

INVENTOR(S): Sebti, Said M.; Hamilton, Andrew D.; Augeri, David J.; Barr, Kenneth J.; Donner, Bernard G.; Fakhoury, Stephen A.; Janowick, David A.; Kalvin, Douglas M.; Larsen, John J.; Liu, Gang; O'Connor, Stephen J.; Rosenberg, Saul H.; Shen, Wang; Swenson, Rolf E.; Sorensen, Bryan K.; Sullivan, Gerard M.; Szczepankiewicz, Bruce G.; Tasker, Andrew S.; Wasick, James T.; Winn, Martin

PATENT ASSIGNEE(S): University of Pittsburgh, USA

SOURCE: PCT Int. Appl., 504 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850030	A1	19981112	WO 1998-US9297	19980507
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
TW 492955	B	20020701	TW 1998-87107182	19980715
TW 541302	B	20030711	TW 1998-87107183	19980715

PRIORITY APPLN. INFO.: US 1997-852858 A 19970507

OTHER SOURCE(S): MARPAT 130:14261

AB Compds. R3-Z-L1-aryl [aryl is a benzene ring having certain substituents R1, R2, R4; L1 is absent or is L4NR5L5, L4OL5, L4S(O)mL5 (m = 0-2), etc., where L4 and L5 are absent or alkylene, alkenylene, R5 is H, alkanoyl; Z is a covalent bond, O, S(O)q (q = 0-2), NH or imino; R3 = H, aryl, fluorenyl, heterocyclyl, cycloalkyl, etc.] were prepared as inhibitors of protein isoprenyl transferases. Thus, N-[4-(2,4-dioxohexahydro-1,3,5-triazin-2-yl)-2-phenylbenzoyl]methionine was prepared and showed 41% inhibition of farnesyltransferase at 1x10<sup>-6</sup> M.

IT 215920-11-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(inhibitors of protein isoprenyl transferases)

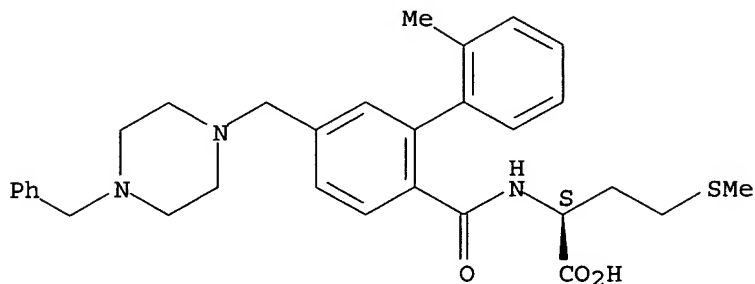
RN 215920-11-9 HCAPLUS

CN L-Methionine, N-[[2'-methyl-5-[[4-(phenylmethyl)-1-



piperazinyl)methyl][1,1'-biphenyl]-2-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 32 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:398242 HCAPLUS

DOCUMENT NUMBER: 129:67800

TITLE: Preparation of N-benzylpiperazine derivatives and their pharmaceutical compositions as anti-ischemic agents

INVENTOR(S): Wierzbicki, Michel; Boussard, Marie-Francoise; Labidalle, Serge; Guyot, Daniel; Rolland, Yves; Tillement, Jean-Paul; Testa, Bernard; Crevat, Aime

PATENT ASSIGNEE(S): Adir et Compagnie, Fr.

SOURCE: Eur. Pat. Appl., 22 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

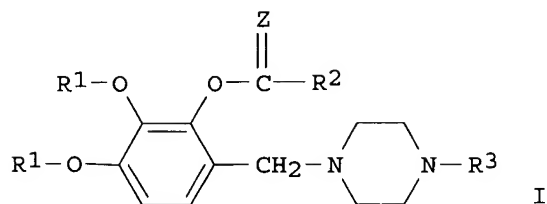
LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 847999	A1	19980617	EP 1997-402934	19971204
EP 847999	B1	20010321		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
FR 2757164	A1	19980619	FR 1996-15415	19961216
FR 2757164	B1	19990122		
AT 199902	E	20010415	AT 1997-402934	19971204
ES 2157541	T3	20010816	ES 1997-402934	19971204
PT 847999	T	20010830	PT 1997-402934	19971204
ZA 9711253	A	19980623	ZA 1997-11253	19971215
JP 10175967	A2	19980630	JP 1997-344823	19971215
US 5849745	A	19981215	US 1997-990611	19971215
CA 2225780	AA	19980616	CA 1997-2225780	19971216
CA 2225780	C	20021119		
NO 9705903	A	19980617	NO 1997-5903	19971216
AU 9748422	A1	19980618	AU 1997-48422	19971216
AU 720803	B2	20000615		
CN 1192436	A	19980909	CN 1997-107273	19971216
BR 9706360	A	19990601	BR 1997-6360	19971216
GR 3035855	T3	20010831	GR 2001-400707	20010511
PRIORITY APPLN. INFO.:			FR 1996-15415	A 19961216

OTHER SOURCE(S): CASREACT 129:67800; MARPAT 129:67800  
GI



AB Disclosed are N-benzylpiperazine derivs. I [R1 = linear or branched C1-6 alkyl; Z = O or S; R2 = linear or branched C1-8 alkyl (un)substituted by carboxy group or C1-6 linear or branched alkoxy carbonyl, or R2 = linear or branched C1-6 alkoxy, various (un)substituted Ph, (un)substituted C3-7 cycloalkyl, 4-(2,3-dithiacyclopent-1-yl)butyl, pyridyl, amino group (un)substituted with 1-2 linear or branched C1-6 alkyls, or R2 = various 6-acetoxy-2,5,7,8-tetramethylchroman-2-yl derivs.; R3 = H, C3-7 cycloalkyl, -CHO, various (un)substituted Ph, pyridyl, or various (un)substituted linear or branched C1-20 alkyl], its isomers, and pharmaceutically acceptable salts. A process for the preparation of I is also disclosed. The preparation involves reaction of 1,2-(R1O)2-3-(HO)C6H3 with an N-substituted piperazine in the presence of CH2O, O-acylation of the trimetazidine derivative, then subsequent possible conversion to a thioester with Lawesson's reagent. Compds. I are useful as anti-ischemic agents (for treatment of chronic cellular ischemia, acute cerebral, cardiac or peripheral ischemia), for the treatment of chronic neurodegenerative diseases (e.g., Alzheimer's or Parkinson's disease), and for improving preservation of transplant organs. Pharmaceutical formulations containing I are also disclosed (1 example).

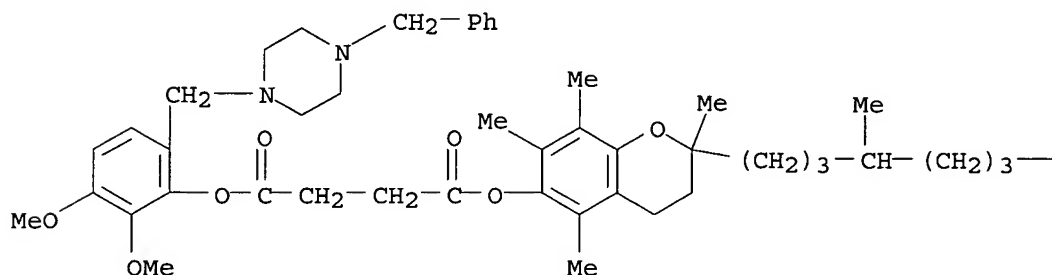
IT 208934-79-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-benzylpiperazine derivs. as anti-ischemic agents)

RN 208934-79-6 HCAPLUS

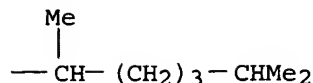
CN Butanedioic acid, 3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-yl 2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]methyl]phenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



● 2 HCl

PAGE 1-B



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 33 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:627054 HCAPLUS

DOCUMENT NUMBER: 127:293722

TITLE: New polyesters with photosensitive backbones based on the triazene unit

AUTHOR(S): Nuyken, Oskar; Dahn, Ulrich

CORPORATE SOURCE: Lehrstuhl fur Makromolekulare Stoffe, Institut fur Technische Chemie der TU Munchen, Garching, 85747, Germany

SOURCE: Journal of Polymer Science, Part A: Polymer Chemistry (1997), 35(14), 3017-3025  
CODEN: JPACEC; ISSN: 0887-624X

PUBLISHER: Wiley

DOCUMENT TYPE: Journal

LANGUAGE: English

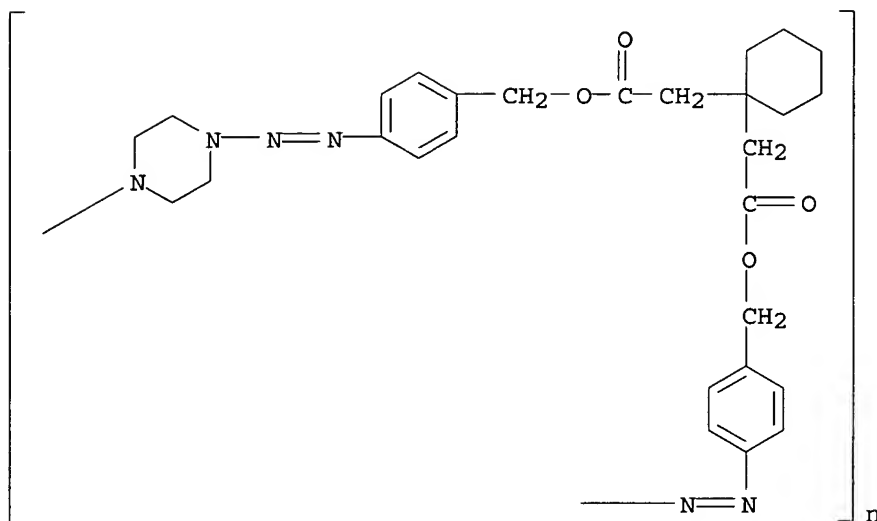
AB The synthesis of photosensitive polymers that contain the triazeno group (Ph-N=N-NR<sub>2</sub>) as a sensitive unit in their backbone is reported. The synthesis pathway consists of difunctional alcs. incorporating the photosensitive unit that react with diacyl derivs. to give the resp. polyesters. Upon irradiation, the photosensitive chromophores both in monomeric and polymeric surroundings are cleaved fast and irreversibly, as shown in photolytic studies and their kinetic evaluations. Thermogravimetric investigations indicate the loss of nitrogen being the initial thermal decomposition step and exhibit stabilities sufficient for the requirements in applications as photoresists.

IT 197249-69-7P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (preparation and characterization of polyesters with photosensitive backbones based on the triazene unit)

RN 197249-69-7 HCAPLUS

CN Poly[1,4-piperazinediylazo-1,4-phenylenemethyleneoxy(1-oxo-1,2-ethanediyl)cyclohexylidene(2-oxo-1,2-ethanediyl)oxymethylene-1,4-phenyleneazo] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 34 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:587697 HCAPLUS

DOCUMENT NUMBER: 127:262704

TITLE: Preparation of piperazine-containing oximes as matrix metalloproteinase inhibitors and pharmaceuticals containing them

INVENTOR(S): Tomiyama, Takeshi; Tomiyama, Itaru; Imamaki, Takeyuki; Takeuchi, Satoshi; Okura, Yasushi

PATENT ASSIGNEE(S): Kotobuki Seiyaku Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

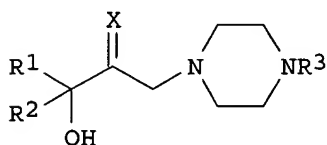
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09227539	A2	19970902	JP 1996-29566	19960216
PRIORITY APPLN. INFO.:			JP 1996-29566	19960216
OTHER SOURCE(S):	MARPAT	127:262704		

GI



I

AB Title compds. I [R1, R2 = (substituted) Ph, benzyl, phenethyl, thienyl; R3 = lower alkyl, (substituted) benzyl; X = NOR4; R4 = H, lower alkyl, lower acyl] or their salts, useful for treatment and/or prevention of diseases

caused by degradation of extracellular matrix by matrix metalloproteinases (MMPs), are prepared by halogenation of HOCHR<sub>1</sub>R<sub>2</sub>Ac (II; R<sub>1</sub>, R<sub>2</sub> = same as I), treating 3,3-substituted 3-hydroxy-1-halogenopropan-2-ones with 1-substituted piperazines, treating I (X = O) with R<sub>4</sub>ONH<sub>2</sub> (R<sub>4</sub> = H, lower alkyl), and optional reaction with R<sub>4</sub>Cl (R<sub>4</sub> = lower acyl). I show high oral activity. II (R<sub>1</sub> = R<sub>2</sub> = Ph) was brominated and treated with N-benzylpiperazine to give I (R<sub>1</sub> = R<sub>2</sub> = Ph, R<sub>3</sub> = benzyl, X = O), which was treated with HONH<sub>2</sub>.HCl in EtOH in the presence of NEt<sub>3</sub> under reflux for 15 h to give 77.2% I (R<sub>1</sub> = R<sub>2</sub> = Ph, R<sub>3</sub> = benzyl, X = NOH) (III). III in vitro inhibited MMP-2 from human sarcoma cell with IC<sub>50</sub> of 0.0011 μM.

IT 196108-24-4P 196108-25-5P

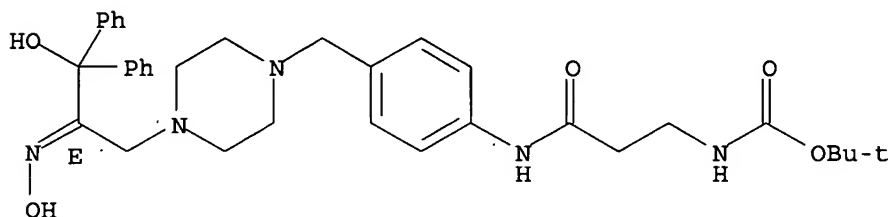
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperazine-containing oximes as matrix metalloproteinase inhibitors)

RN 196108-24-4 HCAPLUS

CN Carbamic acid, [3-[[[4-[[[3-hydroxy-2-(hydroxyimino)-3,3-diphenylpropyl]-1-piperazinyl]methyl]phenyl]amino]-3-oxopropyl]-, 1,1-dimethylethyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

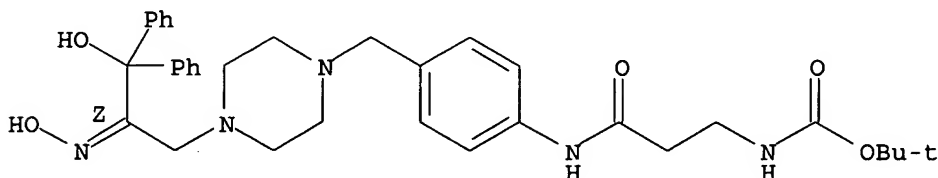


●2 HCl

RN 196108-25-5 HCAPLUS

CN Carbamic acid, [3-[[[4-[[[3-hydroxy-2-(hydroxyimino)-3,3-diphenylpropyl]-1-piperazinyl]methyl]phenyl]amino]-3-oxopropyl]-, 1,1-dimethylethyl ester, dihydrochloride, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

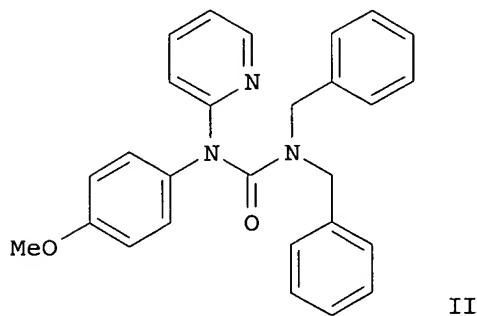


●2 HCl

L12 ANSWER 35 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:537574 HCAPLUS  
 DOCUMENT NUMBER: 127:161697  
 TITLE: 2-Amino heterocycles and their therapeutic uses as  
 leukotriene biosynthesis inhibitors  
 INVENTOR(S): Es-Sayed, Mazen; Yamamoto, Masaru; Frobel, Klaus;  
 Poll, Chris; Grix, Suzanna; Tudhope, Stephen  
 PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany  
 SOURCE: PCT Int. Appl., 275 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9724328	A1	19970710	WO 1996-EP5643	19961216
W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, IL, IS, JP, KE, KP, KR, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9713728	A1	19970728	AU 1997-13728	19961216
PRIORITY APPLN. INFO.:			GB 1995-26560	A 19951227
			WO 1996-EP5643	W 19961216
OTHER SOURCE(S):		MARPAT 127:161697		
GI				



AB 2-Amino heterocycles R<sub>1</sub>R<sub>2</sub>NCOR<sub>3</sub> [I; R<sub>1</sub> = H, Me, (un)substituted 6-membered aromatic heterocycle containing ≤2 N atoms and optionally benzo-fused; R<sub>2</sub> = (un)substituted adamantyl, cycloalkyl, pyridyl, Ph, CH<sub>2</sub>Ph, tetralin-5-yl, 2-norbornyl, 1-azabicyclo[2.2.2]oct-3-yl; or NR<sub>1</sub>R<sub>2</sub> forms α-carboline residue; R<sub>3</sub> = (un)substituted or cyclic amino groups linked via a bond, carbonyl, or alkylene group] are disclosed. I can be used for the production of medicaments which inhibit leukotriene synthesis (in particular LTB<sub>4</sub>), and are especially useful for the treatment and control of respiratory diseases and inflammatory processes (no data). For instance, condensation of 2-chloropyridine with 4-MeOC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> at 150° gave 2-(4-methoxyanilino)pyridine, which reacted with ClCO<sub>2</sub>CCl<sub>3</sub> and then HN(CH<sub>2</sub>Ph)<sub>2</sub> in dioxane at 60° to give title compound II plus a byproduct.

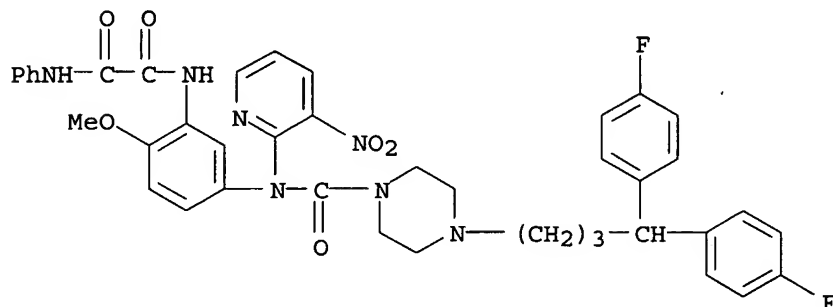
IT 193556-85-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-amino heterocycles as leukotriene biosynthesis inhibitors)

RN 193556-85-3 HCAPLUS

CN Ethanediamide, N-[5-[[[4-[4,4-bis(4-fluorophenyl)butyl]-1-piperazinyl]carbonyl](3-nitro-2-pyridinyl)amino]-2-methoxyphenyl]-N'-phenyl- (9CI) (CA INDEX NAME)



L12 ANSWER 36 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:926097 HCAPLUS

DOCUMENT NUMBER: 123:340182

TITLE: Preparation of hydroxamic acid derivative for inhibiting proliferation of smooth muscle cells and medicinal preparation containing the same

INVENTOR(S): Isozaki, Masashi; Kasukawa, Hiroaki; Nakazawa, Keiichi; Houki, Keiko

PATENT ASSIGNEE(S): Terumo K K, Japan

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

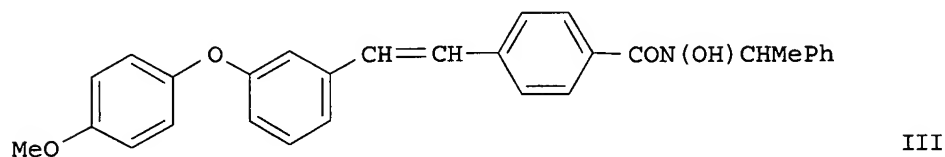
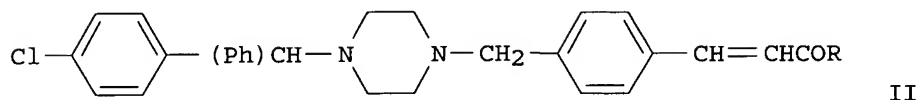
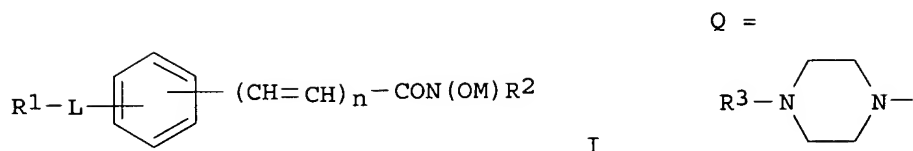
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9513264	A1	19950518	WO 1994-JP1870	19941104
W: US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 07278086	A2	19951024	JP 1994-251094	19941017
PRIORITY APPLN. INFO.:			JP 1993-278168	A 19931108
			JP 1994-22475	A 19940221

OTHER SOURCE(S): MARPAT 123:340182

GI



AB Hydroxamic acid derivs. [I; R<sup>1</sup> = Ph, aryloxyphenyl, Q; wherein R<sup>3</sup> = aryl or aryl-C1-4 alkyl; L = C1-8 alkylene, C2-8 alkenylene, (CH<sub>2</sub>)<sub>m</sub>O (wherein m = an integer 0-4), CO; n = 0 or 1; R<sup>2</sup> = H, C1-4 alkyl, aryl-C1-4 alkyl; M = H, alkanoyl, alkoxy carbonyl, a medically acceptable cation], having the effect of suppressing smooth muscle fiber growth and useful as vascular wall thickening preventives, post-percutaneous transluminal coronary angioplasty (PTCA) restenosis preventives, and even antiarteriosclerotic agents, are prepared. Thus, cinnamic acid derivative (II; R = OH) was stirred with oxalyl chloride and DMF in CH<sub>2</sub>Cl<sub>2</sub> for 2h and the reaction solution was added dropwise to a solution of N-methylhydroxylamine hydrochloride and Et<sub>3</sub>N in aqueous THF, followed by stirring the resulting mixture at room temperature

for 2 h

to give 62.3% N-hydroxy-p-piperazinylmethylcinnamamide II (R = NMeOH). This compound and N-hydroxybenzamide derivative (III) in vitro showed IC<sub>50</sub> of 2.0 + 10<sup>-7</sup> mol for specifically inhibiting the proliferation of smooth muscle cells of a rat thoracic aorta.

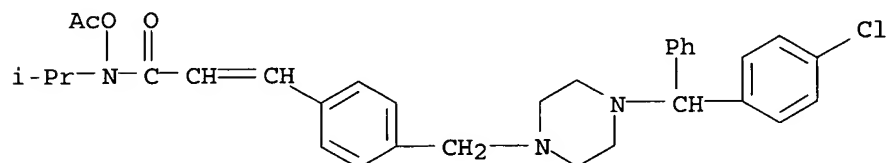
IT 170429-94-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate for preparation of hydroxamic acid derivative for inhibiting proliferation of smooth muscle cells)

RN 170429-94-4 HCAPLUS

CN 2-Propenamide, N-(acetyloxy)-3-[4-[4-[4-(4-chlorophenyl)phenylmethyl]-1-piperazinyl]methyl]phenyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of hydroxamic acid deriv. for inhibiting proliferation of



smooth muscle cells

L12 ANSWER 37 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:807930 HCAPLUS

DOCUMENT NUMBER: 123:198828

TITLE: Preparation of N-(phenoxyethyl)-N'-(diphenylbutyl)piperazines as antiretrovirals.

INVENTOR(S): Wild, Hanno; Bender, Wolfgang; Haebich, Dieter; Raddatz, Siegfried; Roeben, Wolfgang; Seidel, Peter-Rudolf; Hansen, Jutta; Paessens, Arnold

PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

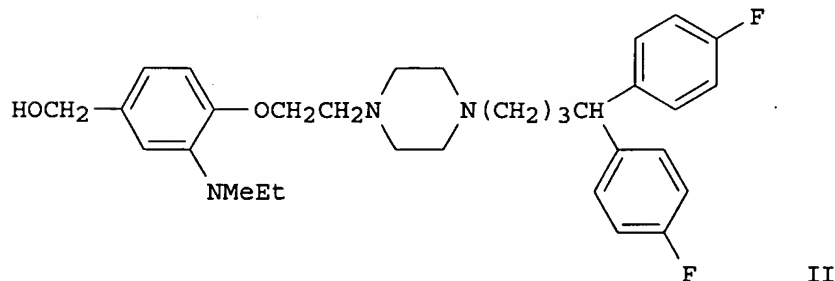
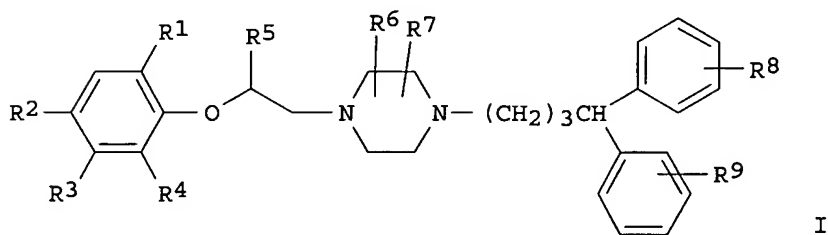
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 623605	A2	19941109	EP 1994-106319	19940422
EP 623605	A3	19950301		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 4314962	A1	19941110	DE 1993-4314962	19930506
AU 9460562	A1	19941110	AU 1994-60562	19940419
AU 678815	B2	19970612		
JP 06329644	A2	19941129	JP 1994-115939	19940502
CA 2122787	AA	19941107	CA 1994-2122787	19940503
ZA 9403099	A	19950113	ZA 1994-3099	19940505
HU 70837	A2	19951128	HU 1994-1331	19940505
CN 1097745	A	19950125	CN 1994-104911	19940506
PRIORITY APPLN. INFO.:			DE 1993-4314962	A 19930506
OTHER SOURCE(S):	MARPAT 123:198828			
GI				



AB Title compds. [I; R1-R4 = H, NO<sub>2</sub>, halo, CO<sub>2</sub>H, OH, CHO, alkoxy, alkoxy carbonyl, CF<sub>3</sub>, Ph, hydroxyalkyl, NR<sub>10</sub>R<sub>11</sub>, COA; R<sub>2</sub>R<sub>3</sub>, R<sub>3</sub>R<sub>4</sub> = atoms to complete 5-7 membered carbocyclic rings; A = NR<sub>12</sub>CHR<sub>13</sub>(CH<sub>2</sub>)<sub>a</sub>COR<sub>14</sub>; R<sub>10</sub>, R<sub>11</sub> = H, Ph, PhCH<sub>2</sub>, protecting group, alkyl; NR<sub>10</sub>R<sub>11</sub> = 5-7 membered saturated heterocyclyl; R<sub>12</sub> = H, alkyl; R<sub>13</sub> = H, aryl, cycloalkyl, (substituted) alkyl; R<sub>14</sub> = OH, alkoxy; R<sub>5</sub> = H, alkyl, CO<sub>2</sub>R<sub>18</sub>, COA; R<sub>1</sub>R<sub>5</sub> = atoms to form a 5-6 membered heterocyclyl; R<sub>18</sub> = H, alkyl, protecting group; R<sub>6</sub>, R<sub>7</sub> = H, CO<sub>2</sub>H, (substituted) alkyl, alkoxy carbonyl; R<sub>8</sub>, R<sub>9</sub> = halo, cyano, NO<sub>2</sub>, N<sub>3</sub>, OH], were prepared Thus, title compound II inhibited HIV protease with IC<sub>50</sub> = 0.17 μM.

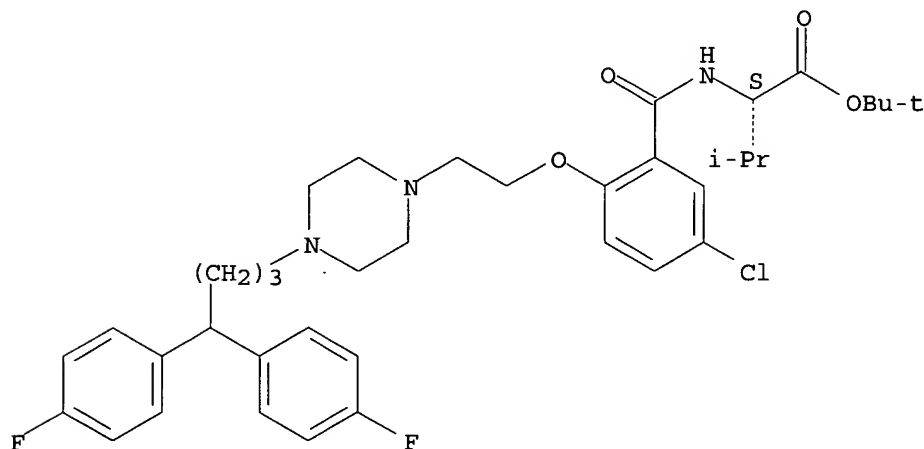
IT 168051-01-2P 168051-02-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-(phenoxyethyl)-N'-(diphenylbutyl)piperazines as antiretrovirals)

RN 168051-01-2 HCAPLUS

CN L-Valine, N-[2-[2-[4-[4,4-bis(4-fluorophenyl)butyl]-1-piperazinyl]ethoxy]-5-chlorobenzoyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

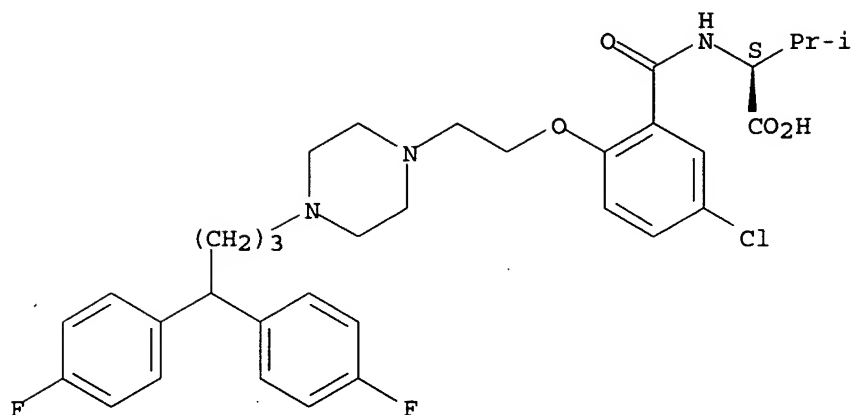
Absolute stereochemistry.



RN 168051-02-3 HCAPLUS

CN L-Valine, N-[2-[2-[4-[4,4-bis(4-fluorophenyl)butyl]-1-piperazinyl]ethoxy]-5-chlorobenzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 38 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:735221 HCAPLUS

DOCUMENT NUMBER: 123:144637

TITLE: Preparation of peptide inhibitors of HIV protease.

INVENTOR(S): Higashida, Susumu; Sakurai, Mitsuya; Yabe, Yuichiro; Nishihgaki, Takashi; Komai, Tomoaki; Handa, Hiroshi

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 354 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

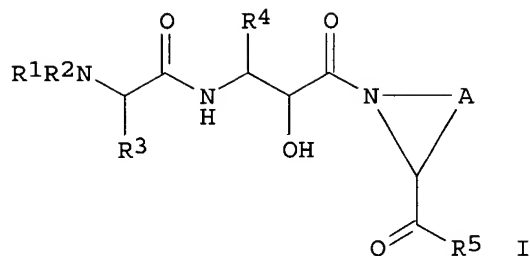
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 587311	A1	19940316	EP 1993-306258	19930806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AU 9344438	A1	19940210	AU 1993-44438	19930805
AU 662434	B2	19950831		
ZA 9305697	A	19940310	ZA 1993-5697	19930805
IL 106600	A1	19970930	IL 1993-106600	19930805
CA 2103536	AA	19940208	CA 1993-2103536	19930806
NO 9302813	A	19940208	NO 1993-2813	19930806
HU 64774	A2	19940228	HU 1993-2286	19930806
RU 2106357	C1	19980310	RU 1993-50122	19930806
KR 177838	B1	19990401	KR 1993-15304	19930806
CN 1091432	A	19940831	CN 1993-117625	19930807
JP 06100533	A2	19940412	JP 1993-197311	19930809
US 5629406	A	19970513	US 1994-227588	19940414
PRIORITY APPLN. INFO.:			JP 1992-211746	A 19920807
			US 1993-102467	B1 19930805

OTHER SOURCE(S): MARPAT 123:144637

GI



AB Title compds. [I; R1 = H, alkyl, aralkyl, CORa, CORb, CSRa, CSRb, SO2Rb, CONHRb, CSNHRb, CONRbRb, CSNRbRb; R2 = H, alkyl; R3 = H, alkylidene, substituted alkyl, Rb; R4 = (substituted) alkyl, cycloalkyl, aryl; R5 = RbO, RbRbN, RbHN, aralkyloxycarbonyloxy, aralkyloxycarbonylamino, (CH2)pD(CH2)r; B, D = bond, CO, O, S, NH, CH2:CH2, NHCO; m, n, p, r = 0-5; A = (CH2)mB(CH2)n; Ra = alkoxy, aralkyloxy, aryloxy, alkoxy carbonyl; Rb = (substituted) alkyl, cycloalkyl, heterocyclyl, aryl, arylalkenyl] and pharmaceutically acceptable salts, esters, and prodrugs thereof, were prepared. Thus, (4S)-1-[(2S,3S)-3-[N2-(2-quinoxalinecarbonyl)asparaginy]amino-2-hydroxy-4-phenylbutyryl]-N-tert-butyl-4-chloroprolinamide, prepared by solution phase methods, inhibited release of virus from HIV-infected Molt 4 cells with IC50 = 0.39 µg/mL, vs. >20 µg/mL for RO 31-8959.

IT **166383-04-6P 166383-28-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of peptide inhibitors of HIV protease)

RN 166383-04-6 HCAPLUS

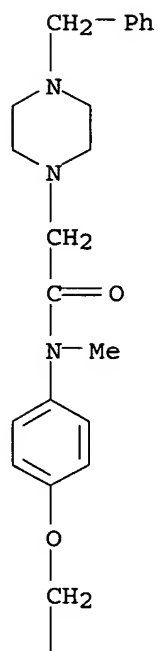
CN L-Prolinamide, N2-[[4-[methyl[[4-(phenylmethyl)-1-piperazinyl]acetyl]amino]phenoxy]acetyl]-L-asparaginy]-(2S,3S)-2-hydroxy-4-phenyl-3-aminobutanoyl-N-(1,1-dimethylethyl)-, monoacetate (salt) (9CI)  
(CA INDEX NAME)

CM 1

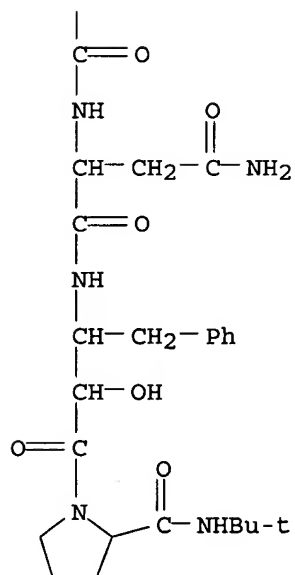
CRN 166383-03-5

CMF C45 H60 N8 O8

PAGE 1-A

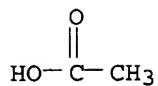


PAGE 2-A



CM 2

CRN 64-19-7  
CMF C2 H4 O2

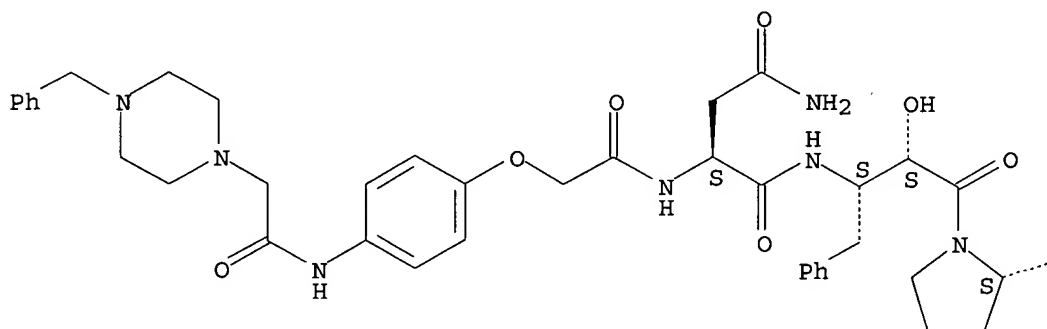


RN 166383-28-4 HCAPLUS

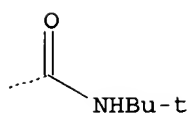
CN L-Prolinamide, N2-[[4-[[[4-(phenylmethyl)-1-piperazinyl]acetyl]amino]phenoxy]acetyl]-L-asparaginy]- (2S,3S)-2-hydroxy-4-phenyl-3-aminobutanoyl-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L12 ANSWER 39 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:667081 HCAPLUS

DOCUMENT NUMBER: 123:55917

TITLE: Antithrombogenic piperazine derivatives.

INVENTOR(S): Gante, Joachim; Raddatz, Peter; Juraszyk, Horst;  
Bernotat-Danielowski, Sabine; Melzer, Guido

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

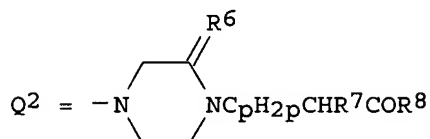
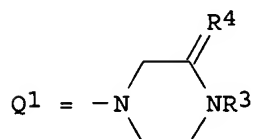
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 608759	A2	19940803	EP 1994-100709	19940119
EP 608759	A3	19941005		
EP 608759	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
DE 4302485	A1	19940804	DE 1993-4302485	19930129
JP 06271549	A2	19940927	JP 1994-3451	19940118
AT 204570	E	20010915	AT 1994-100709	19940119
ES 2162825	T3	20020116	ES 1994-100709	19940119
PT 608759	T	20020228	PT 1994-100709	19940119
SK 281842	B6	20010806	SK 1994-68	19940120
AU 9454702	A1	19940804	AU 1994-54702	19940125
AU 670649	B2	19960725		
CN 1099759	A	19950308	CN 1994-101127	19940125
CN 1056141	B	20000906		
CZ 288122	B6	20010411	CZ 1994-163	19940125
CA 2114361	AA	19940730	CA 1994-2114361	19940127
NO 9400308	A	19940801	NO 1994-308	19940128
NO 312550	B1	20020527		
ZA 9400615	A	19940913	ZA 1994-615	19940128
HU 70042	A2	19950928	HU 1994-249	19940128
PL 172716	B1	19971128	PL 1994-302069	19940128
RU 2154639	C2	20000820	RU 1994-2323	19940128
US 5908843	A	19990601	US 1994-189385	19940131
GR 3036838	T3	20020131	GR 2001-401700	20011009
PRIORITY APPLN. INFO.:			DE 1993-4302485	A 19930129
OTHER SOURCE(S):	MARPAT	123:55917		
GI				



AB The title compds. Y(CmH<sub>2</sub>mCHR<sub>1</sub>)nCO(NHCHR<sub>2</sub>CO)rZ [I; R<sub>1</sub>, R<sub>2</sub> = (un)substituted PhCH<sub>2</sub>, etc.; Y = Q<sub>1</sub>, 4-R<sub>5</sub>C<sub>6</sub>H<sub>4</sub>; Z = Q<sub>1</sub>, Q<sub>2</sub>, etc.; R<sub>3</sub> = H, H<sub>2</sub>NC(:NH)NH; R<sub>4</sub>, R<sub>6</sub> = H<sub>2</sub>, :O; R<sub>7</sub> = R<sub>1</sub>; R<sub>8</sub> = OH, NHOH, etc.; m = 0-4; n, r = 0, 1; p = 0-2], useful as antithrombotics (no data), antineoplastic agents (no data), antiatherosclerotics (no data), etc., are prepared and I-containing formulations

presented. Thus, 3-[4-(4-guanidinobenzoyl)-2-oxo-1-piperazinyl]propionic acid, m.p. 110° (decomposition), was prepared

IT 164784-45-6P 164784-47-8P 164784-48-9P  
 164784-50-3P 164784-51-4P 164784-52-5P  
 164784-53-6P 164784-57-0P 164784-58-1P  
 164784-59-2P 164784-62-7P 164784-63-8P  
 164784-64-9P 164784-65-0P 164784-66-1P  
 164784-67-2P 164784-68-3P 164784-69-4P

164784-70-7P 164784-71-8P 164784-72-9P

164784-73-0P 164784-76-3P

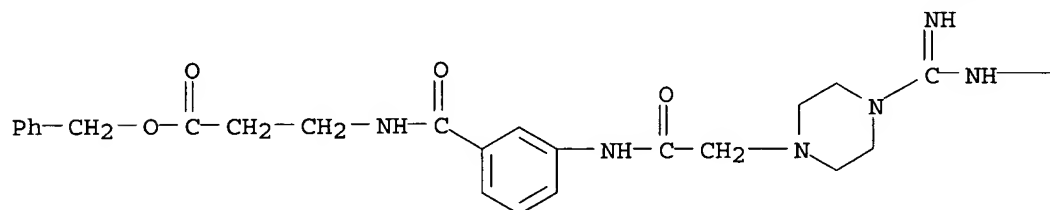
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of antithrombogenic piperazines)

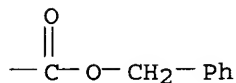
RN 164784-45-6 HCAPLUS

CN  $\beta$ -Alanine, N-[3-[[[4-[imino[(phenylmethoxy)carbonyl]amino]methyl]-1-piperazinyl]acetyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



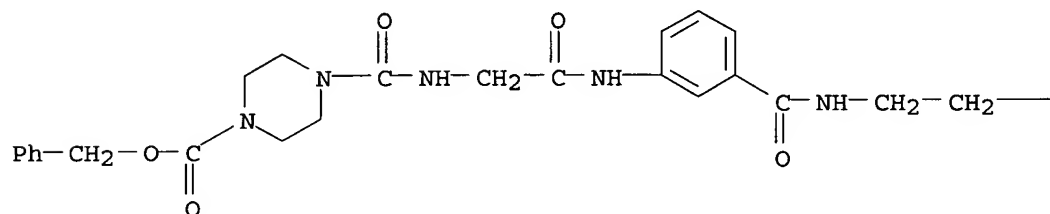
PAGE 1-B



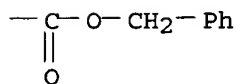
RN 164784-47-8 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[[2-oxo-2-[[3-[[[3-oxo-3-(phenylmethoxy)propyl]amino]carbonyl]phenyl]amino]ethyl]amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

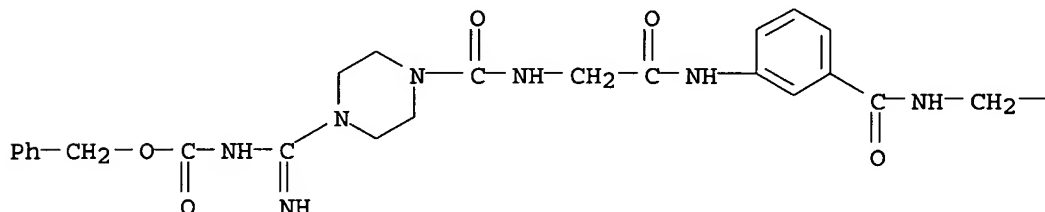


RN 164784-48-9 HCAPLUS

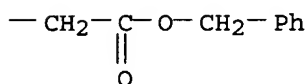


CN  $\beta$ -Alanine, N-[3-[[[[[4-[imino[[{(phenylmethoxy)carbonyl]amino]methyl]-1-piperazinyl]carbonyl]amino]acetyl]amino]benzoyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

PAGE 1-A



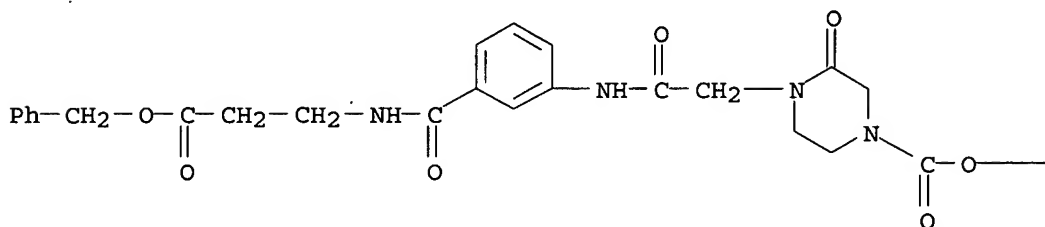
PAGE 1-B



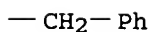
RN 164784-50-3 HCAPLUS

CN 1-Piperazinecarboxylic acid, 3-oxo-4-[2-oxo-2-[[3-[[[3-oxo-3-(phenylmethoxy)propyl]amino]carbonyl]phenyl]amino]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



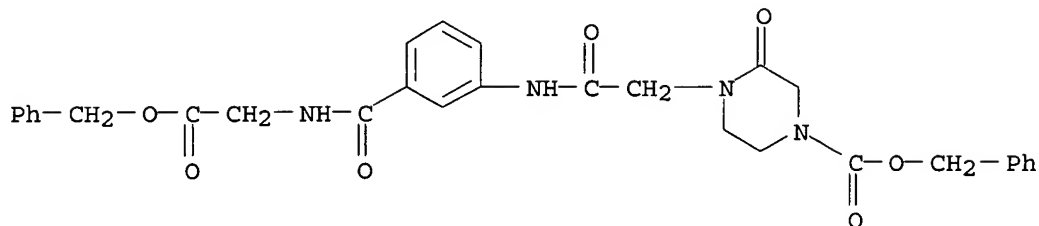
PAGE 1-B



RN 164784-51-4 HCAPLUS

CN 1-Piperazinecarboxylic acid, 3-oxo-4-[2-oxo-2-[[3-[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]phenyl]amino]ethyl]-, phenylmethyl

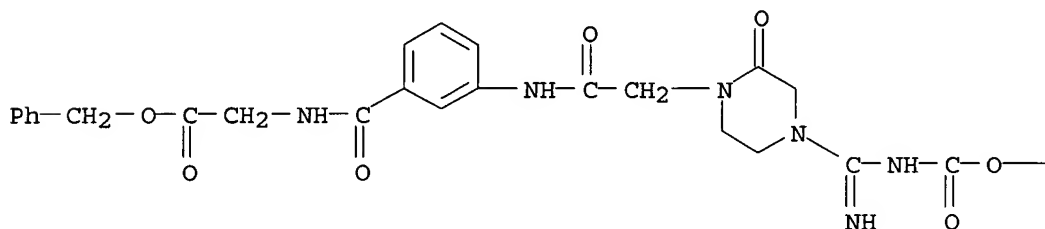
ester (9CI) (CA INDEX NAME)



RN 164784-52-5 HCAPLUS

CN Glycine, N-[3-[[[4-[imino[(phenylmethoxy)carbonyl]amino]methyl]-2-oxo-1-piperazinyl]acetyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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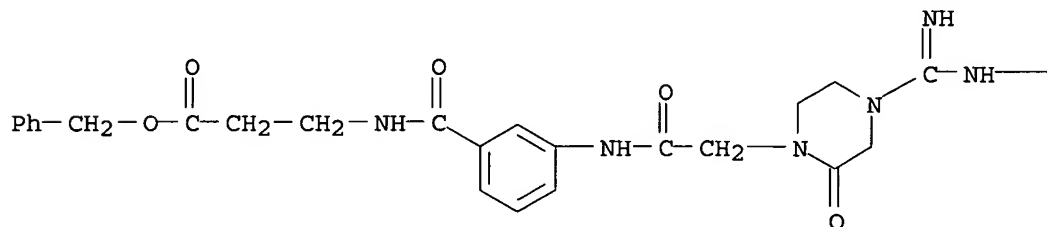
PAGE 1-B

—CH<sub>2</sub>—Ph

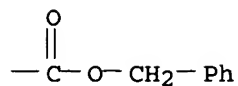
RN 164784-53-6 HCAPLUS

CN β-Alanine, N-[3-[[[4-[imino[(phenylmethoxy)carbonyl]amino]methyl]-2-oxo-1-piperazinyl]acetyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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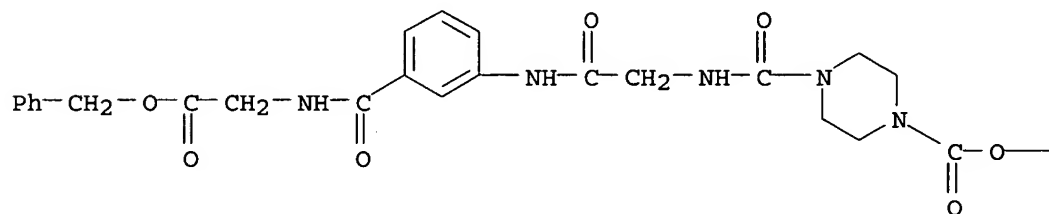
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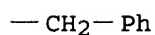
RN 164784-57-0 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[[2-oxo-2-[[3-[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]phenyl]amino]ethyl]amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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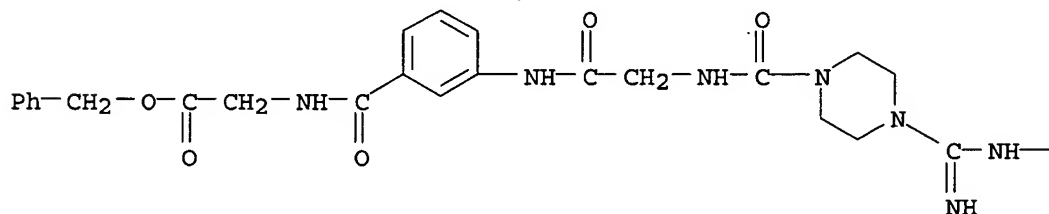
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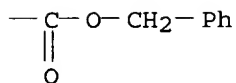
RN 164784-58-1 HCAPLUS

CN Glycine, N-[3-[[[[[4-[imino[(phenylmethoxy)carbonyl]amino)methyl]-1-piperazinyl]carbonyl]amino]acetyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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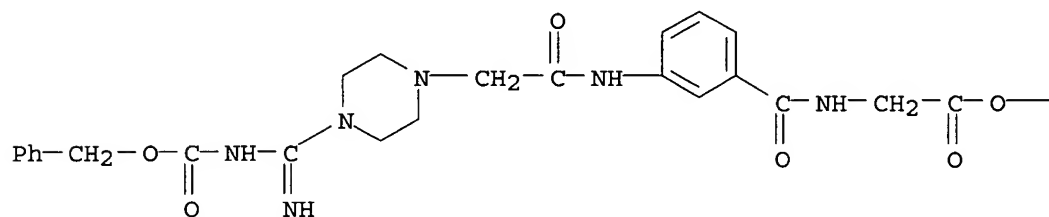
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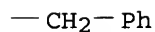
RN 164784-59-2 HCAPLUS

CN Glycine, N-[3-[[[4-[imino[(phenylmethoxy)carbonyl]amino]methyl]-1-piperazinyl]acetyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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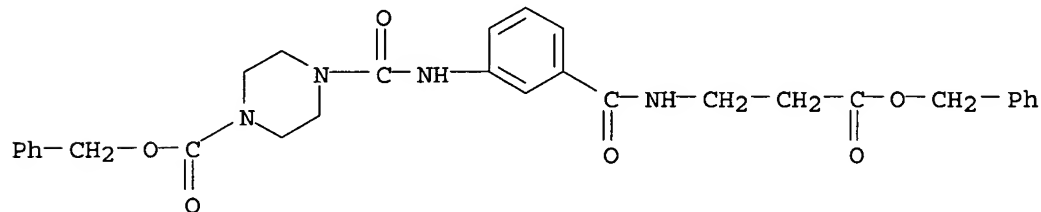


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RN 164784-62-7 HCAPLUS

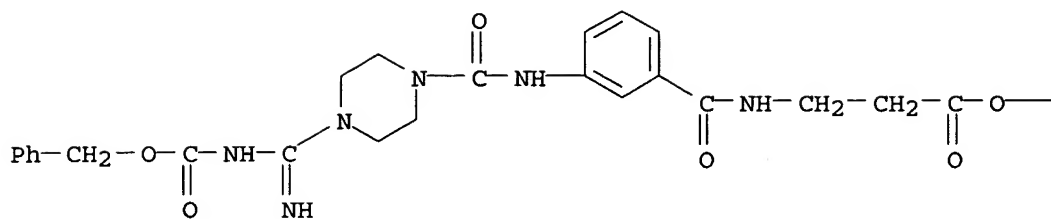
CN 1-Piperazinecarboxylic acid, 4-[[[3-[[[3-oxo-3-(phenylmethoxy)propyl]amino]carbonyl]phenyl]amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 164784-63-8 HCAPLUS

CN β-Alanine, N-[3-[[[4-[imino[(phenylmethoxy)carbonyl]amino]methyl]-1-piperazinyl]carbonyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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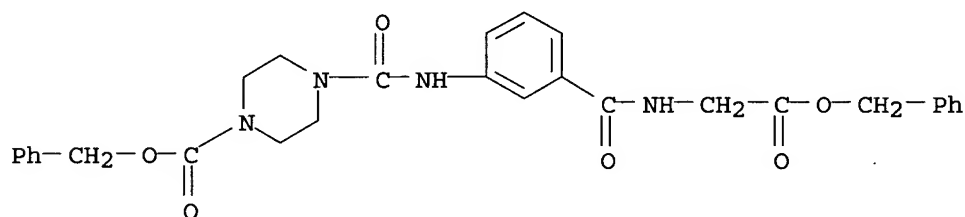


PAGE 1-B

—CH<sub>2</sub>—Ph

RN 164784-64-9 HCAPLUS

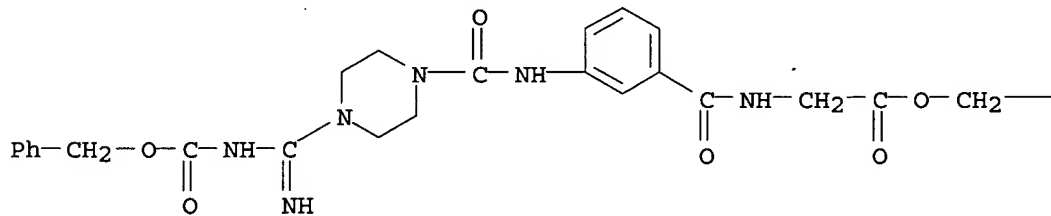
CN 1-Piperazinecarboxylic acid, 4-[[[3-[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]phenyl]amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 164784-65-0 HCAPLUS

CN Glycine, N-[3-[[[4-[imino[[[2-oxo-2-(phenylmethoxy)ethyl]amino]methyl]-1-piperazinyl]carbonyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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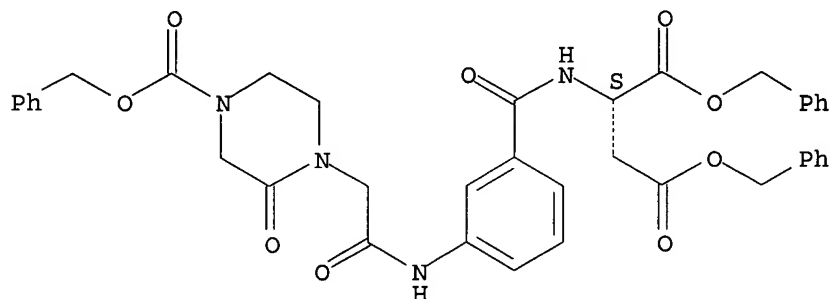
PAGE 1-B

— Ph

RN 164784-66-1 HCAPLUS

CN L-Aspartic acid, N-[3-[[[2-oxo-4-[(phenylmethoxy)carbonyl]-1-piperazinyl]acetyl]amino]benzoyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

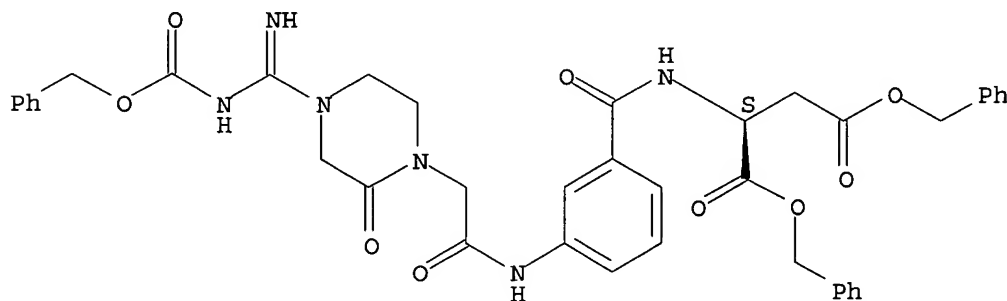
Absolute stereochemistry.



RN 164784-67-2 HCAPLUS

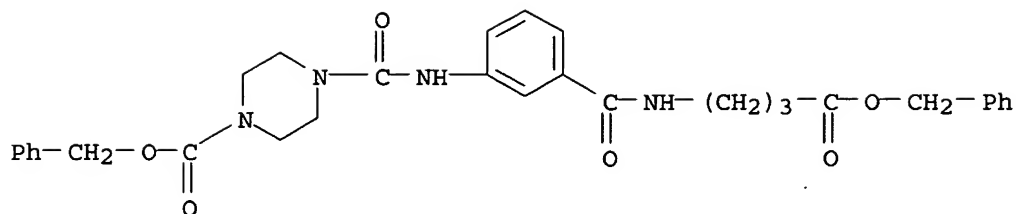
CN L-Aspartic acid, N-[3-[[[4-[imino[[[(phenylmethoxy)carbonyl]amino]methyl]-2-oxo-1-piperazinyl]acetyl]amino]benzoyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 164784-68-3 HCAPLUS

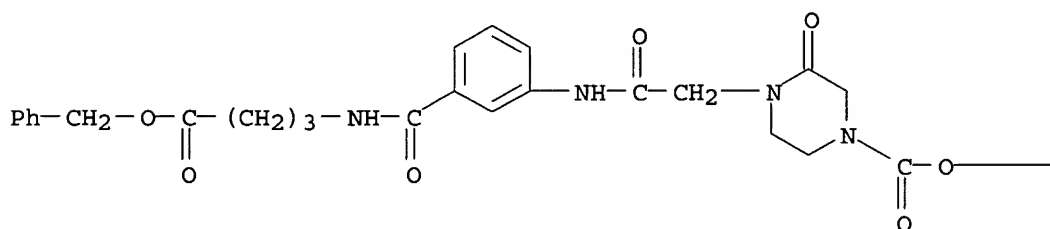
CN 1-Piperazinecarboxylic acid, 4-[[[3-[[[4-oxo-4-(phenylmethoxy)butyl]amino]carbonyl]phenyl]amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 164784-69-4 HCAPLUS

CN 1-Piperazinecarboxylic acid, 3-oxo-4-[2-oxo-2-[[3-[[[4-oxo-4-(phenylmethoxy)butyl]amino]carbonyl]phenyl]amino]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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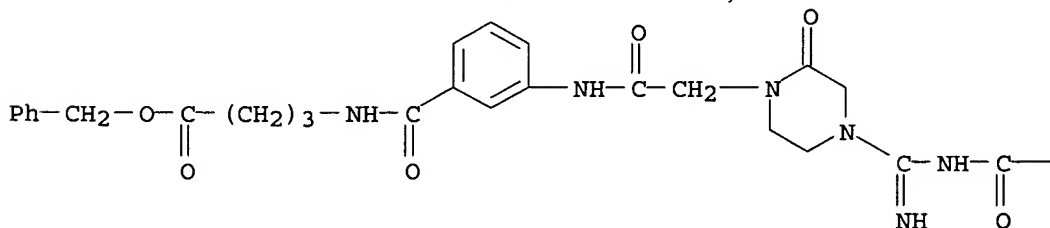
PAGE 1-B

—CH<sub>2</sub>—Ph

RN 164784-70-7 HCAPLUS

CN Butanoic acid, 4-[[3-[[[4-[imino[[[phenylmethoxy]carbonyl]amino]methyl]-2-oxo-1-piperazinyl]acetyl]amino]benzoyl]amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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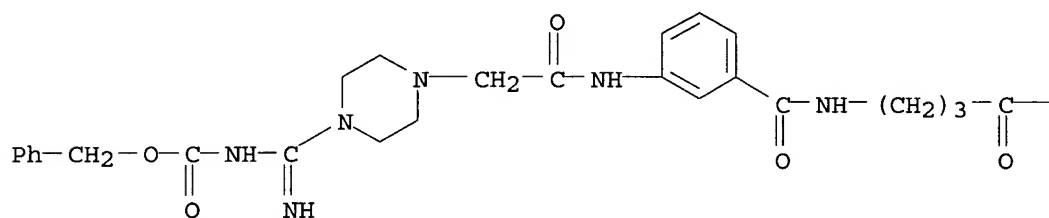


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— O—CH<sub>2</sub>—Ph

RN 164784-71-8 HCAPLUS  
 CN Butanoic acid, 4-[[3-[[[4-[imino[(phenylmethoxy)carbonyl]amino]methyl]-1-piperazinyl]acetyl]amino]benzoyl]amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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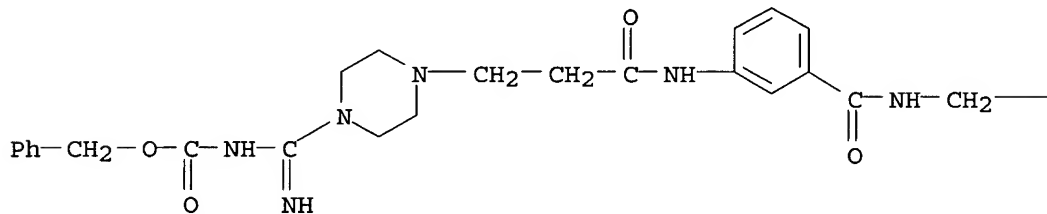


PAGE 1-B

— O—CH<sub>2</sub>—Ph

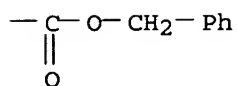
RN 164784-72-9 HCAPLUS  
 CN Glycine, N-[3-[[3-[4-[imino[(phenylmethoxy)carbonyl]amino]methyl]-1-piperazinyl]-1-oxopropyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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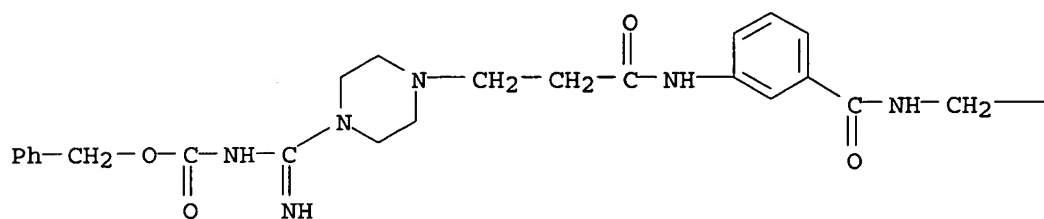


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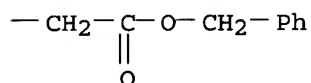


RN 164784-73-0 HCAPLUS  
 CN  $\beta$ -Alanine, N-[3-[[[3-[4-[imino[[[(phenylmethoxy)carbonyl]amino]methyl]-1-piperazinyl]-1-oxopropyl]amino]benzoyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

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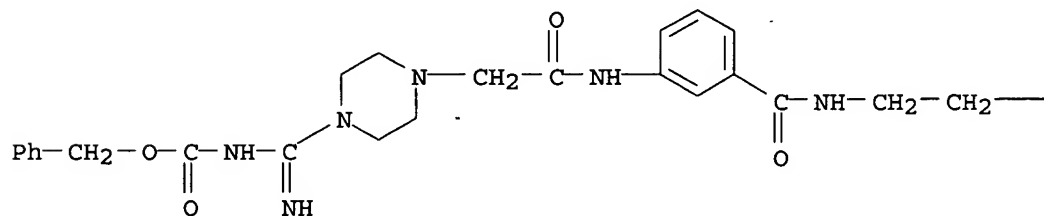


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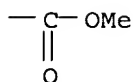


RN 164784-76-3 HCAPLUS  
 CN  $\beta$ -Alanine, N-[3-[[[4-[imino[[[(phenylmethoxy)carbonyl]amino]methyl]-1-piperazinyl]acetyl]amino]benzoyl]-, methyl ester (9CI) (CA INDEX NAME)

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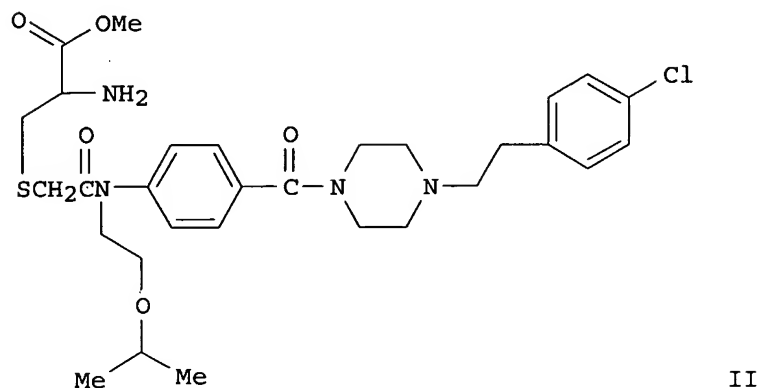
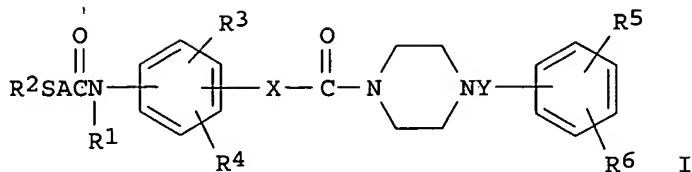


PAGE 1-B



L12 ANSWER 40 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1995:324534 HCAPLUS  
 DOCUMENT NUMBER: 122:106523  
 TITLE: Substituted [[(Piperazinylcarbonyl)phenyl]amino]alkyl  
 Thioethers  
 INVENTOR(S): Ferrini, Pier Giorgio  
 PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.  
 SOURCE: Eur. Pat. Appl., 27 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 606824	A1	19940720	EP 1993-810906	19931224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5380726	A	19950110	US 1993-170110	19931220
AU 9352611	A1	19940721	AU 1993-52611	19931221
JP 06247949	A2	19940906	JP 1993-351780	19931229
CA 2112786	AA	19940716	CA 1994-2112786	19940104
FI 9400154	A	19940716	FI 1994-154	19940112
ZA 9400280	A	19940705	ZA 1994-280	19940114
NO 9400135	A	19940718	NO 1994-135	19940114
HU 70936	A2	19951128	HU 1994-118	19940114
PRIORITY APPLN. INFO.:			CH 1993-115	A 19930115
OTHER SOURCE(S):	MARPAT 122:106523			
GI				



AB The title compds., I (R1 = H, alkyl, etc.; R2 = alkyl, carboxy, etc.; R3, R4 = H, alkyl, halo, etc.; R5, R6 = H, alkyl, halo, amino, etc.; A, X, Y = alkanediyl) were disclosed. A specifically claimed example compound is (R)-1-[4-[[[2-amino-2-(methoxycarbonyl)ethyl]thio]acetyl](2-isopropoxyethyl)amino]benzoyl]-4-[2-(4-chlorophenyl)ethyl]piperazine (II). The title compds. were prepared from amino acids, such as cysteine or glutathione. I were claimed for the treatment of diseases mediated by interleukin-1, however, pharmacol. test data were not shown.

IT 160580-41-6P

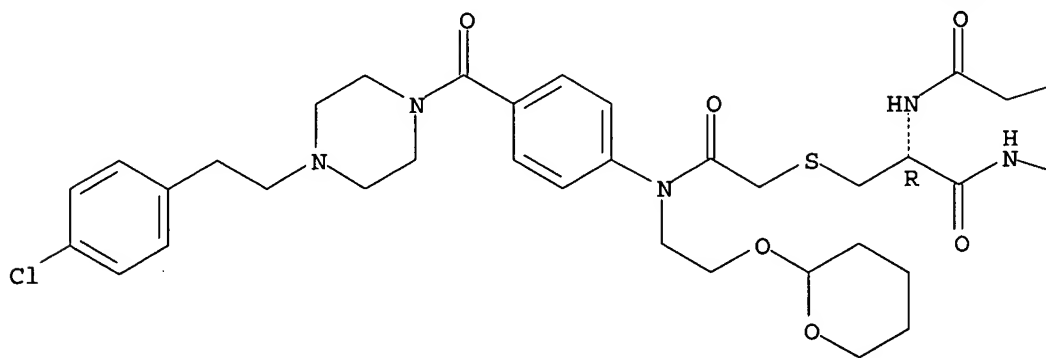
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as intermediate for [[(piperazinylcarbonyl)phenyl]amino]alkyl thioether)

RN 160580-41-6 HCAPLUS

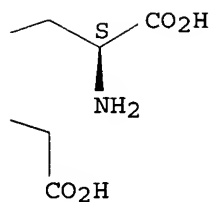
CN Glycine, N-[S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]amino]-2-oxoethyl]-N-L-γ-glutamyl-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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IT 160580-42-7P 160580-43-8P 160580-44-9P  
 160580-45-0P 160580-46-1P 160580-47-2P  
 160580-48-3P 160580-49-4P 160580-50-7P  
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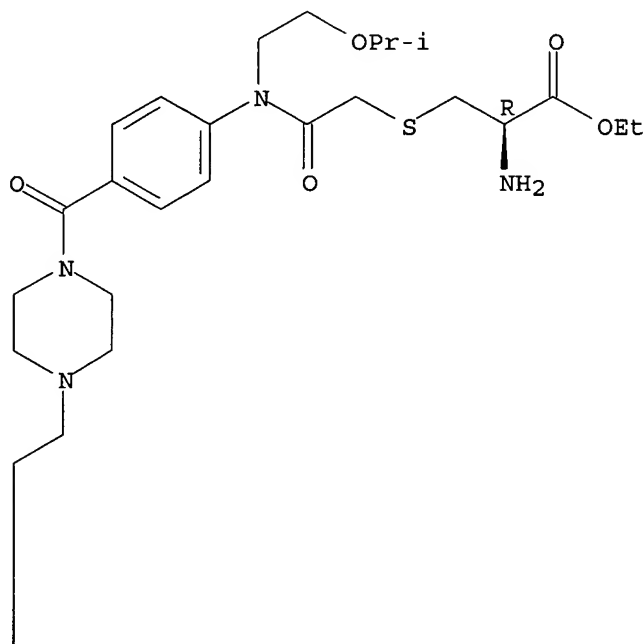
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, for treatment of diseases mediated by interleukin-1)

RN 160580-42-7 HCAPLUS

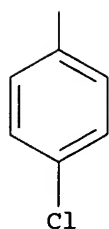
CN L-Cysteine, S- [2- [[4- [[4- [2- (4-chlorophenyl) ethyl] -1-  
 piperazinyl] carbonyl] phenyl] [2- (1-methylethoxy) ethyl] amino] -2-oxoethyl] -,  
 ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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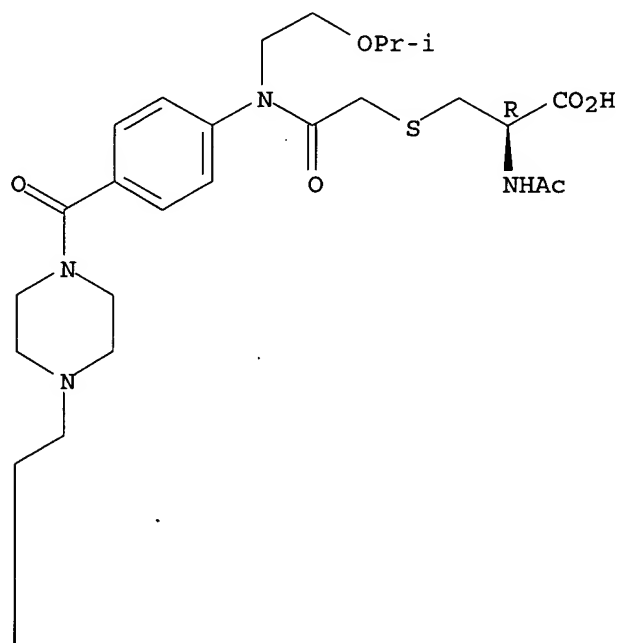
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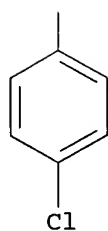
CN L-Cysteine, N-acetyl-S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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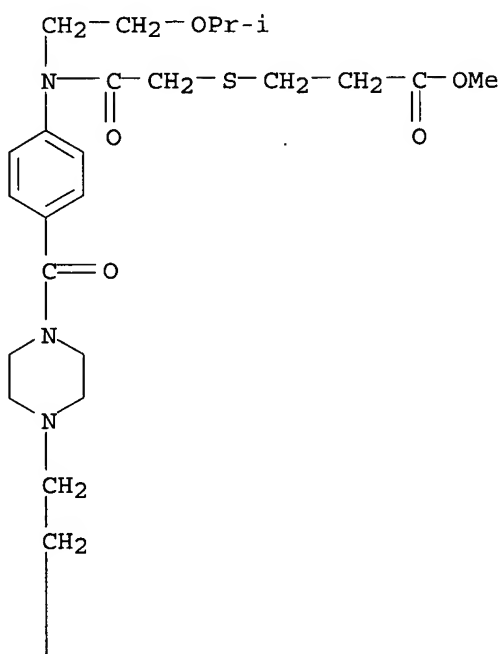
PAGE 2-A



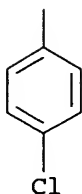
● HCl

RN 160580-44-9 HCAPLUS  
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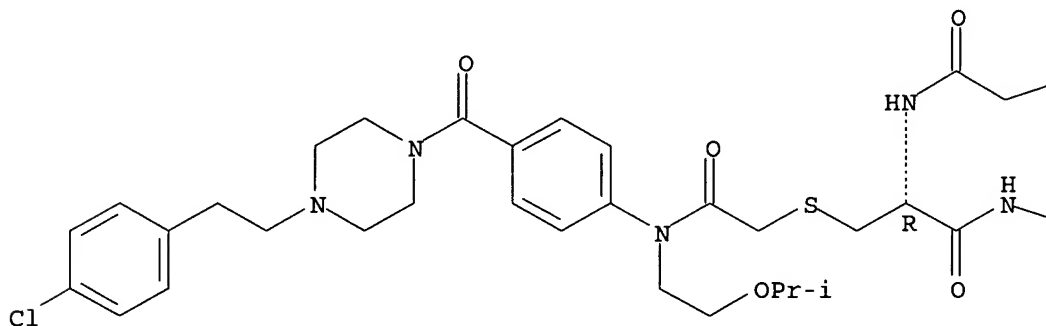


● HCl

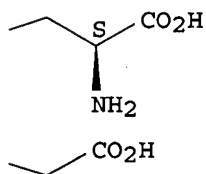
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 CN Glycine, N-[S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-N-L-γ-glutamyl-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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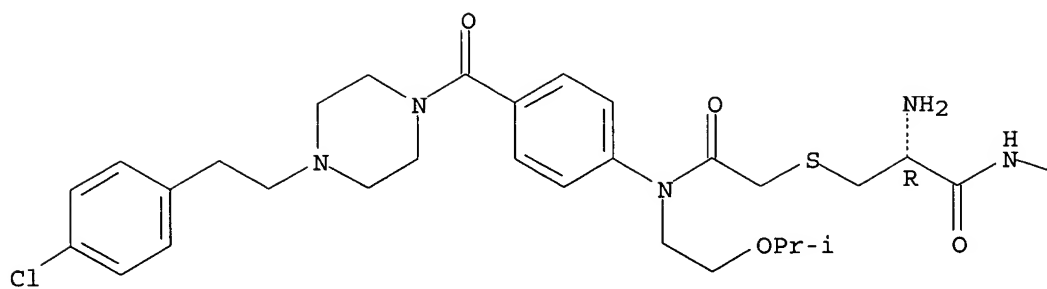
PAGE 1-B



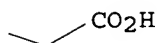
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 CN Glycine, N-[S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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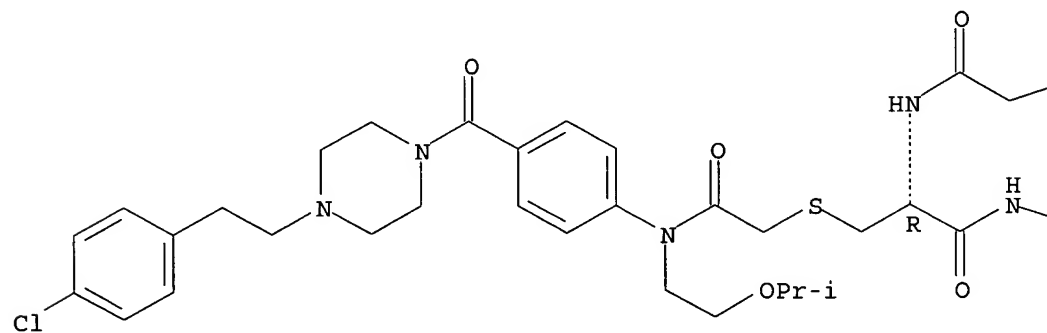
PAGE 1-B



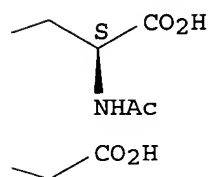
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 CN Glycine, N-(N-(N-acetyl-L-γ-glutamyl)-S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-L-cysteinyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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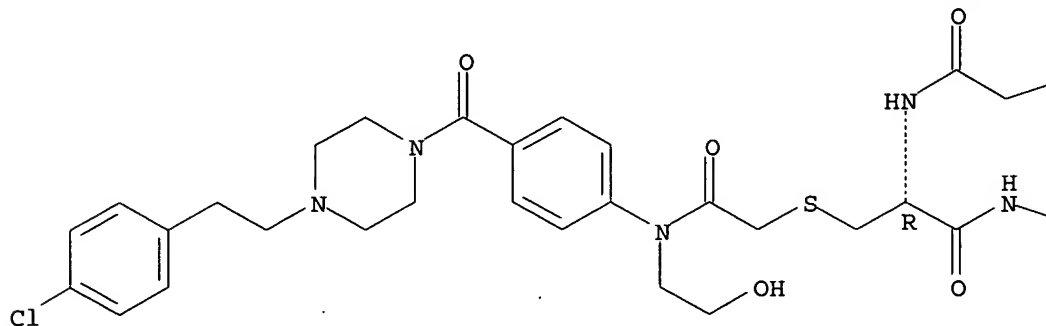




RN 160580-48-3 HCAPLUS  
 CN Glycine, N-[S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl](2-hydroxyethyl)amino]-2-oxoethyl]-L-γ-glutamyl-L-cysteinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

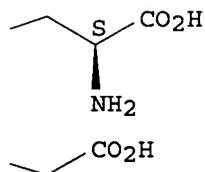
Absolute stereochemistry.

PAGE 1-A



● 2 HCl

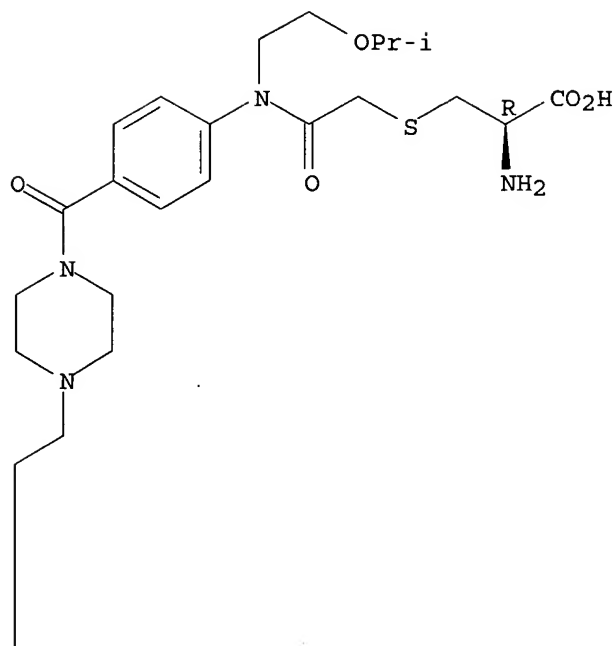
PAGE 1-B



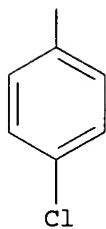
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 CN L-Cysteine, S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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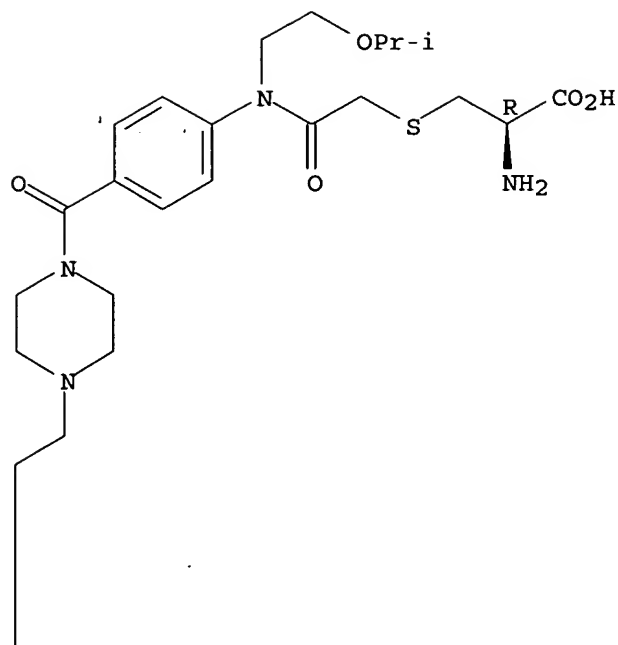


● HCl

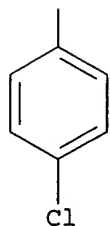
RN 160580-50-7 HCAPLUS  
 CN L-Cysteine, S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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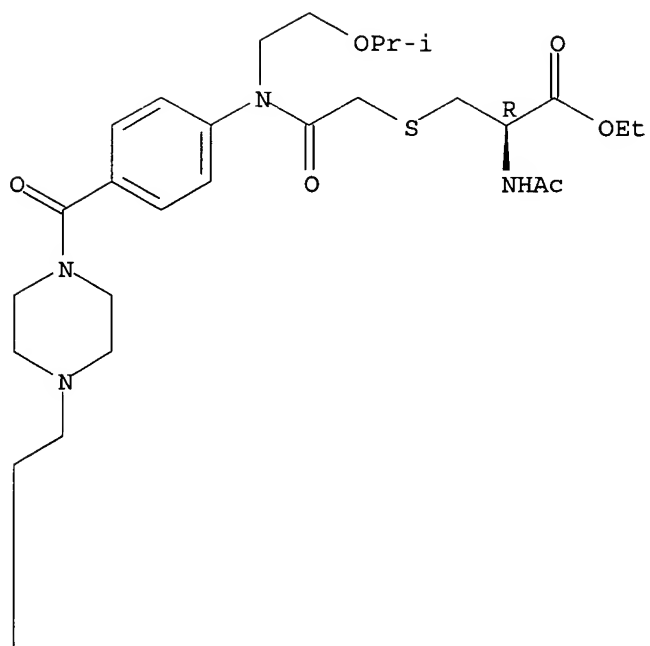


RN 160580-51-8 HCAPLUS

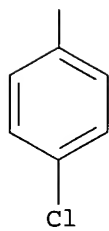
CN L-Cysteine, N-acetyl-S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

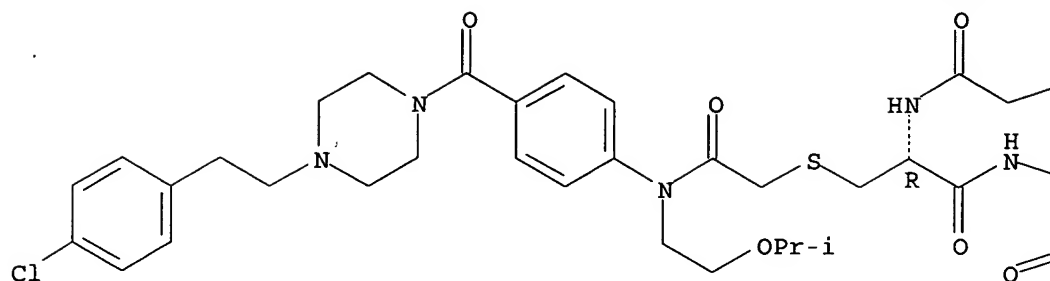


● HCl

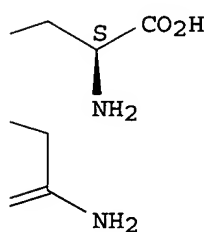
RN 160580-52-9 HCAPLUS  
 CN Glycinamide, L-γ-glutamyl-S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

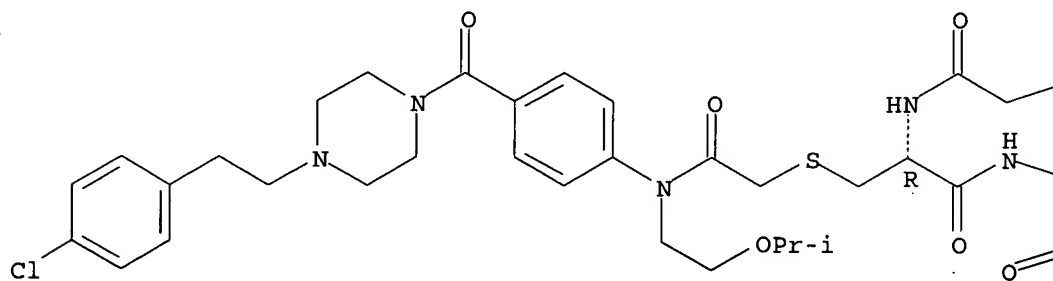


RN 160580-53-0 HCAPLUS

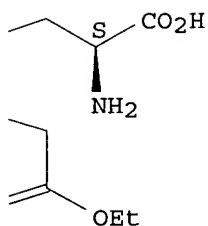
CN Glycine, N- [S- [2- [[4- [[4- [2- (4-chlorophenyl) ethyl] -1-  
piperazinyl] carbonyl] phenyl] [2- (1-methylethoxy) ethyl] amino] -2-oxoethyl] -N-  
L-γ-glutamyl-L-cysteinyl]-, 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



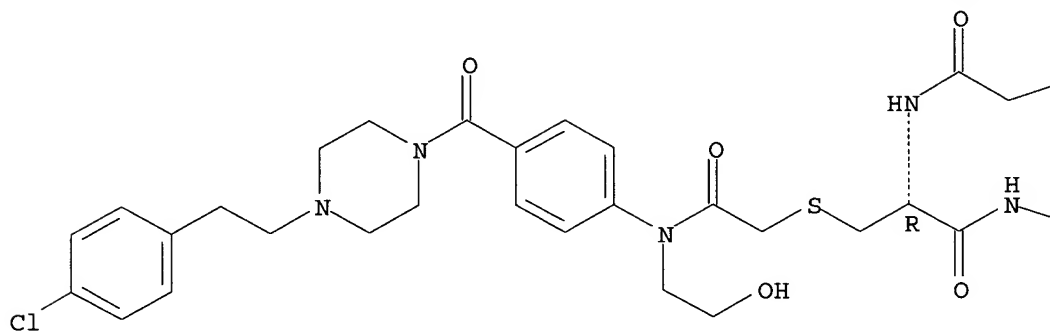
PAGE 1-B



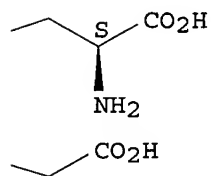
RN 160580-54-1 HCAPLUS  
 CN Glycine, N-[S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl](2-hydroxyethyl)amino]-2-oxoethyl]-N-L-γ-glutamyl-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



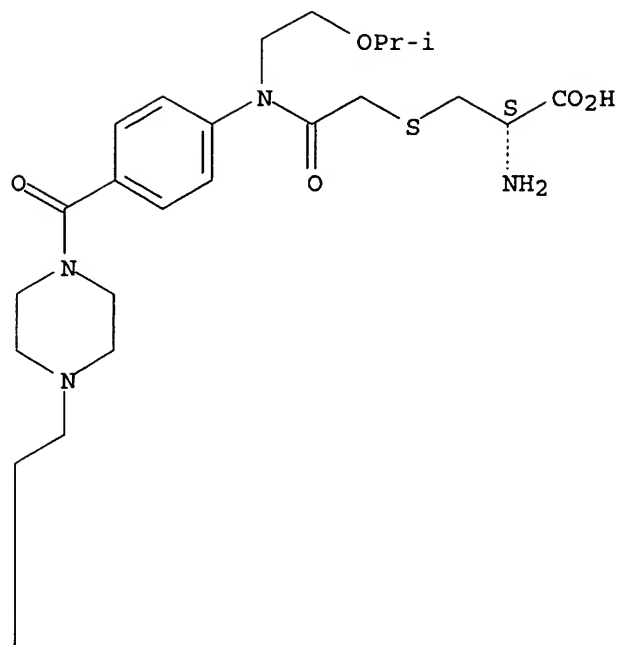
PAGE 1-B



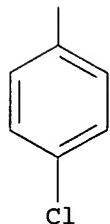
RN 160580-55-2 HCAPLUS  
 CN D-Cysteine, S-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L12 ANSWER 41 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:277045 HCAPLUS

DOCUMENT NUMBER: 122:46487

TITLE: CAT-1 inhibitors, their synthesis, pharmaceutical compositions, and methods of use

INVENTOR(S): Guthrie, Robert W.; Mullin, John G., Jr.; Kachensky, David F.; Kierstead, Richard W.; Tilley, Jefferson W.; Heathers, Guy P.; Higgins, Alan J.; Lemahieu, Ronald A.

PATENT ASSIGNEE(S): Hoffman-La Roche Inc., USA

SOURCE: U.S., 85 pp. Cont.-in-part of U.S. Ser. No. 698, 014, abandoned.

CODEN: USXXAM

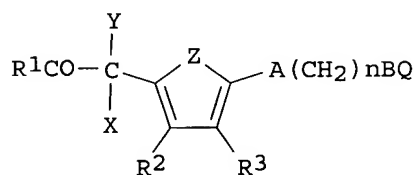
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5344843	A	19940906	US 1992-850620	19920313
RU 2059603	C1	19960510	RU 1992-5011784	19920131
EP 512352	A2	19921111	EP 1992-107135	19920427
EP 512352	A3	19930310		
EP 512352	B1	19960327		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
AT 136018	E	19960415	AT 1992-107135	19920427
AU 9216003	A1	19921112	AU 1992-16003	19920504
AU 653398	B2	19940929		
CA 2068076	AA	19921110	CA 1992-2068076	19920506
ZA 9203279	A	19930127	ZA 1992-3279	19920506
NO 9201840	A	19921110	NO 1992-1840	19920508
HU 63602	A2	19930928	HU 1992-1538	19920508
JP 05279353	A2	19931026	JP 1992-143375	19920508
JP 07107060	B4	19951115		
RO 109938	B1	19950728	RO 1992-622	19920508
BR 9201769	A	19921229	BR 1992-1769	19920511
PRIORITY APPLN. INFO.:			US 1991-698014	B2 19910509
			US 1992-850620	A 19920313
OTHER SOURCE(S):		MARPAT 122:46487		
GI				

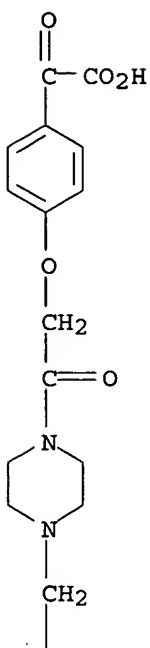


I

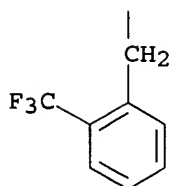
- AB The invention relates to compds. I (R<sub>1</sub> = OH; R<sub>2</sub>, R<sub>3</sub> = H, alkyl, aryl, alkoxy, etc.; X, Y together = O, or one is amino and other is H; Z = S, CR<sub>2</sub>=CR<sub>2</sub>'; A = bond, O, S, SO, CHCH, etc.; B = bond, O, S, SO, etc.; Q = Ph, cyclohexyl, pyridinyl, etc.; n = 1-6) and their pharmaceutically acceptable salts, and when appropriate, enantiomers, racemates, diastereomers or mixts. thereof or geometric isomer or mixts. thereof, and pharmaceutically acceptable salts thereof. The compds. inhibit carnitine acyltransferase 1 (CAT-1) and are therefore useful in the prevention of injury to ischemic tissue, and can limit infarct size, improve cardiac function and prevent arrhythmias during and following a myocardial infarction. 5-[[2-(2-Naphthalenyloxy)ethyl]oxy]-α-oxo-2-thiopheneacetic acid (preparation given) inhibited CAT-1 with an IC<sub>50</sub> = 0.05 μM. Tablet and capsule formulations containing 4-[2-(2-naphthyloxy)ethoxy]-α-oxobenzeneacetic acid are presented.
- IT **146572-66-9P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (synthesis and pharmaceutical compns. and use of carnitine acyltransferase inhibitor compds.)
- RN 146572-66-9 HCAPLUS
- CN Benzeneacetic acid, α-oxo-4-[2-oxo-2-[4-[2-[2-(trifluoromethyl)phenyl]ethyl]-1-piperazinyl]ethoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



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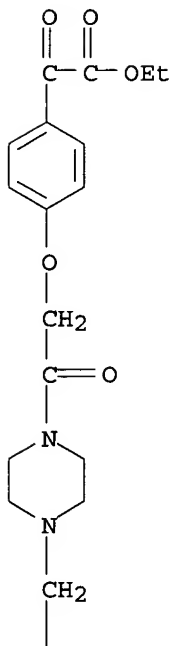
PAGE 2-A



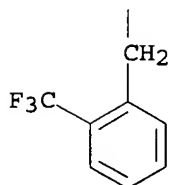
● HCl

IT 145797-87-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (synthesis and pharmaceutical compns. and use of carnitine  
 acyltransferase inhibitor compds.)  
 RN 145797-87-1 HCAPLUS  
 CN Benzeneacetic acid,  $\alpha$ -oxo-4-[2-oxo-2-[4-[2-[2-  
 (trifluoromethyl)phenyl]ethyl]-1-piperazinyl]ethoxy]-, ethyl ester (9CI)  
 (CA INDEX NAME)

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L12 ANSWER 42 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1994:483367 HCAPLUS  
 DOCUMENT NUMBER: 121:83367  
 TITLE: Analgesic diarylmethylpiperazines and piperidines  
 INVENTOR(S): Chang, Kwen Jen; Boswell, Grady Evan; Bubacz, Dulce  
 Garrido; Collins, Mark Allan; Davis, Ann Otstot;  
 Mcnutt, Robert Walton  
 PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK  
 SOURCE: PCT Int. Appl., 214 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 7  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9315062	A1	19930805	WO 1993-GB216	19930202

W: AT, AU, BR, CA, CH, DE, ES, HU, JP, KP, LU, NL, NO, PL, RO, RU, SE, UA, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

AU 9334573	A1	19930901	AU 1993-34573	19930202
AU 675928	B2	19970227		
ZA 9300717	A	19940802	ZA 1993-717	19930202
JP 07503247	T2	19950406	JP 1993-513072	19930202
JP 3109832	B2	20001120		
EP 649414	A1	19950426	EP 1993-914513	19930202
EP 649414	B1	20030416		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

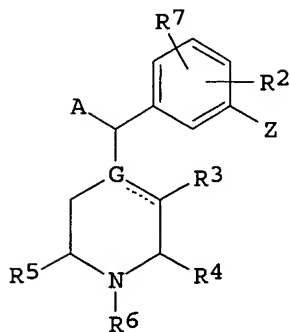
IL 104582	A1	19981030	IL 1993-104582	19930202
AT 237597	E	20030515	AT 1993-914513	19930202
PT 649414	T	20030930	PT 1993-914513	19930202
ES 2197152	T3	20040101	ES 1993-914513	19930202
US 5658908	A	19970819	US 1994-284445	19940803
US 5854249	A	19981229	US 1997-864667	19970528
US 2002052007	A1	20020502	US 2001-957903	20010921

PRIORITY APPLN. INFO.:

GB 1992-2238	A	19920203
WO 1993-GB216	A	19930202
US 1994-284445	A3	19940803
US 1996-658726	A2	19960605
US 1997-887312	A3	19970703
US 1999-352308	A2	19990712

OTHER SOURCE(S): MARPAT 121:83367

GI



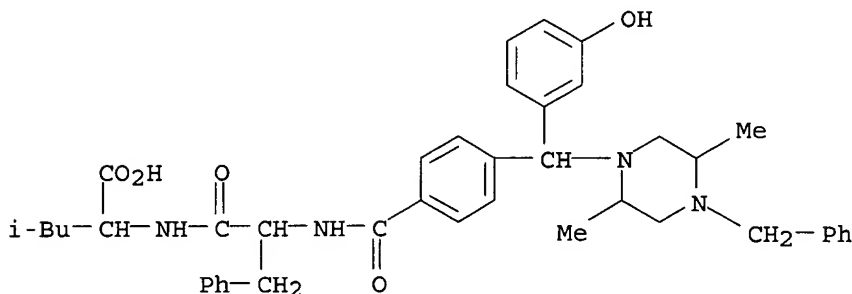
AB The title compds. [I; A = 5- or 6-membered carbocyclic or heterocyclic aromatic ring; G = C, N; R2 = H, halogen, C1-4 alkyl; R3-R5 = H, Me (so long as the total number of Me groups is not greater than 2); R6 = H, C1-6 alkyl, C3-6 cycloalkyl, aralkyl, etc.; R7 = H, F; Z = HO, esters, hydroxymethyl, NH2, carboximides, sulfonimides; R1 = R2 = R7 = F only when Z = OH and G = C when R6 ≠ aralkyl], useful as mu and/or delta receptor opioid compds. for mediating analgesia, are prepared and I-containing formulations presented. Thus, (±)-4-[(α-R)-α-[(2S,5R)]-4-allyl-2,5-dimethyl-1-piperazinyl-3-hydroxybenzyl]-N,N-diethylbenzamide, prepared from 3-bromophenol in a multi-step reaction, demonstrated 50% inhibitory concentration against rat brain delta receptors at 1.8 nM and 50% Mu receptor inhibitory concentration of 15 nM.

IT 155806-55-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation and analgesic activity of)

RN 155806-55-6 HCAPLUS

CN L-Leucine, N-[N-[4-[[2,5-dimethyl-4-(phenylmethyl)-1-piperazinyl](3-hydroxyphenyl)methyl]benzoyl]-L-phenylalanyl]-, [2R-[1(R\*),2 $\alpha$ ,5 $\beta$ ]]- (9CI) (CA INDEX NAME)



L12 ANSWER 43 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:422383 HCAPLUS

DOCUMENT NUMBER: 121:22383

TITLE: silver halide color photographic material

INVENTOR(S): Morigaki, Masakazu; Yamada, Kohzaburoh; Seto, Nobuo;  
Yoshioka, Yasuhiro

PATENT ASSIGNEE(S): Fuji Photo Film Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 102 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 570006	A1	19931118	EP 1993-107890	19930514
EP 570006	B1	19990324		
R: DE, FR, GB, NL				
JP 06027609	A2	19940204	JP 1993-23464	19930120
JP 3101848	B2	20001023		
US 5362617	A	19941108	US 1993-59981	19930512
PRIORITY APPLN. INFO.:			JP 1992-148009	A 19920515
			JP 1993-23464	A 19930120

OTHER SOURCE(S): MARPAT 121:22383

GI For diagram(s), see printed CA Issue.

AB A silver halide color photog. material comprises a support provided thereon at least one layer containing a coupler represented by the formula ACOCHZCONHB wherein A represents a group represented by NR<sub>1</sub>R<sub>2</sub>, I, or II (R<sub>1</sub>, R<sub>2</sub> = an aliphatic, aromatic, or heterocyclic group; Q<sub>1</sub> = an organic group necessary to form a N-containing heterocyclic ring; R<sub>3</sub> = an organic group; Q<sub>2</sub> = an organic group necessary to form a 3- to 6-membered ring; B = an aromatic or heterocyclic group; Z = H or a group capable of splitting off upon coupling reaction with the oxidation product of an aromatic primary amine

developing agent).

IT 155620-21-6 155620-30-7

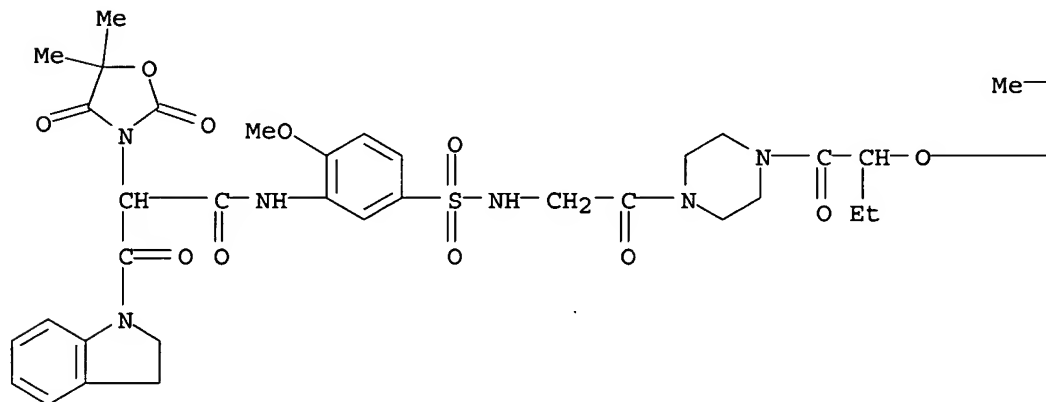
RL: USES (Uses)

(yellow photog. coupler)

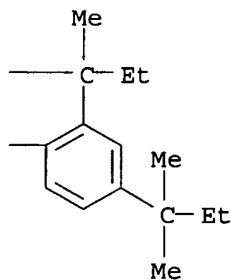
RN 155620-21-6 HCAPLUS

CN 1H-Indole-1-propanamide, N-[5-[[[2-[4-[2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-1-oxobutyl]-1-piperazinyl]-2-oxoethyl]amino]sulfonyl]-2-methoxyphenyl]- $\alpha$ -(5,5-dimethyl-2,4-dioxo-3-oxazolidinyl)-2,3-dihydro- $\beta$ -oxo- (9CI) (CA INDEX NAME)

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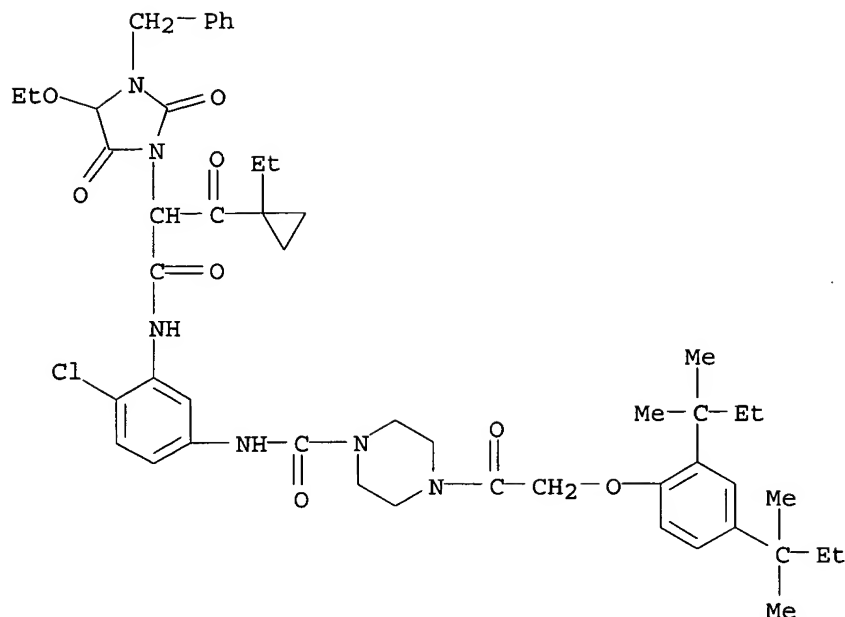


PAGE 1-B



RN 155620-30-7 HCAPLUS

CN 1-Piperazinecarboxamide, 4-[[2,4-bis(1,1-dimethylpropyl)phenoxy]acetyl]-N-[4-chloro-3-[[2-[4-ethoxy-2,5-dioxo-3-(phenylmethyl)-1-imidazolidinyl]-3-(1-ethylcyclopropyl)-1,3-dioxopropyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L12 ANSWER 44 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:580818 HCAPLUS

DOCUMENT NUMBER: 119:180818

TITLE: Preparation of piperazine derivatives as drugs

INVENTOR(S): Kumagai, Kazuhiro; Nagasawa, Masaaki; Takahashi, Hidenori; Abe, Tooru; Omata, Takeshi; Segawa, Yoshihide

PATENT ASSIGNEE(S): Zeria Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

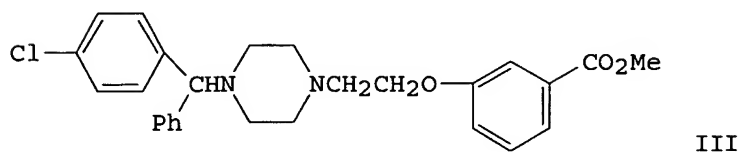
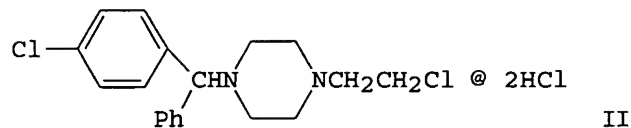
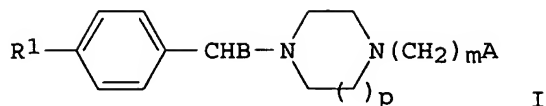
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9302062	A1	19930204	WO 1992-JP833	19920702
W: AU, CA, JP, KR, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
CA 2113449	AA	19930204	CA 1992-2113449	19920702
AU 9222316	A1	19930223	AU 1992-22316	19920702
AU 658656	B2	19950427		
EP 598123	A1	19940525	EP 1992-914249	19920702
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 2767321	B2	19980618	JP 1992-502728	19920702
US 5432179	A	19950711	US 1993-170198	19931230
PRIORITY APPLN. INFO.:			JP 1991-203755	A 19910719
			WO 1992-JP833	A 19920702

OTHER SOURCE(S): MARPAT 119:180818

GI



AB Piperazine derivs. [I; A = (substituted) phenoxy, pyridyloxy, quinolinyloxy, indolinyloxy, etc.; B = Ph, pyridyl; R1 = H, halo; m = 2, 3' p = 1,2], useful as antiallergic, antihistaminic, and antiasthmatic agents, are prepared and formulated. 3-HOC6H4CO2Me was added to a suspension of piperazine salt II and K2CO3 in Me2CO and then refluxed to give 68% III. I showed 52.3-86.4% allergy inhibition at 10 mg/kg orally in rats. I also showed IC50 of 0.14-1.59  $\mu$ M in vitro against histamine in guinea pigs. Granular, tablet, and injection formulations are given.

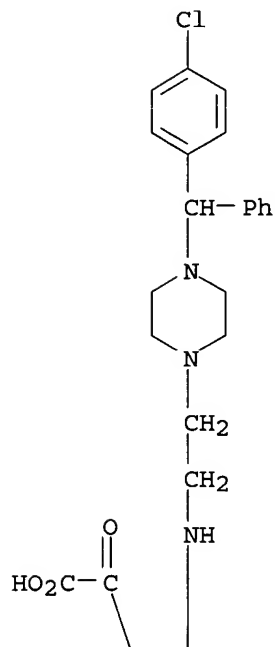
IT 150167-44-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of, as drug)

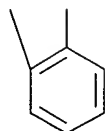
RN 150167-44-5 HCAPLUS

CN Benzeneacetic acid, 2-[[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethyl]amino]- $\alpha$ -oxo-, monosodium salt (9CI) (CA INDEX NAME)

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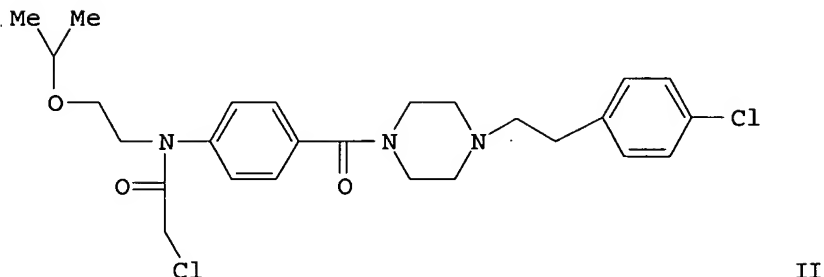
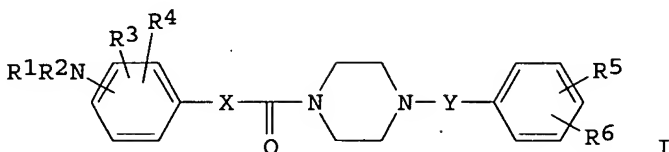
● Na

L12 ANSWER 45 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1993:254960 HCAPLUS  
 DOCUMENT NUMBER: 118:254960  
 TITLE: Preparation of N-(aminoaroyl)-N'-(arylalkyl)piperazines as analgesics  
 INVENTOR(S): Ferrini, Pier Giorgio  
 PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.  
 SOURCE: Eur. Pat. Appl., 30 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 524146	A1	19930120	EP 1992-810525	19920710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
US 5286728	A	19940215	US 1992-913277	19920714
AU 9220317	A1	19930121	AU 1992-20317	19920715
AU 650989	B2	19940707		
CA 2074154	AA	19930120	CA 1992-2074154	19920717
NO 9202853	A	19930120	NO 1992-2853	19920717
ZA 9205359	A	19930331	ZA 1992-5359	19920717
JP 05202014	A2	19930810	JP 1992-190894	19920717
HU 67047	A2	19950130	HU 1992-2359	19920717
PRIORITY APPLN. INFO.:			CH 1991-2160	A 19910719
			CH 1992-1340	A 19920427
OTHER SOURCE(S):			MARPAT 118:254960	
GI				



AB Title compds. [I; R1 = H, alkyl, alkoxyalkyl, aryloxyalkyl, (di)alkylaminoalkyl, etc.; R2 = (substituted) alkenoyl, carbamoyl, carboxycarbonyl, H, alkanoyl, CO<sub>2</sub>H, alkoxy carbonyl, arylalkoxycarbonyl, etc.; R3, R4 = H, alkyl, halo, alkoxy, alkylthio; R5, R6 = H, alkyl, haloalkyl, alkoxy, alkylthio, halo, (di)(alkyl)amino, alkanoylamino; X, Y = bond, alkylene, alkenylene], were prepared Thus, 1-[4-[N-(2-isopropoxyethyl)amino]benzoyl]-4-[2-(4-chlorophenyl)ethyl]piperazine (preparation given) was stirred with K<sub>2</sub>CO<sub>3</sub> and ClCH<sub>2</sub>COCl in PhMe at 45° to give title compound II. HCl. Numerous dosage formulations were prepared containing II or II salts. I inhibited lipopolysaccharide-induced fever in rats with Eb50 = 0.05-3.5 mg/kg orally.

IT 147131-48-4P 147131-49-5P 147131-50-8P  
147131-53-1P 147131-54-2P 147131-61-1P  
147149-07-3P

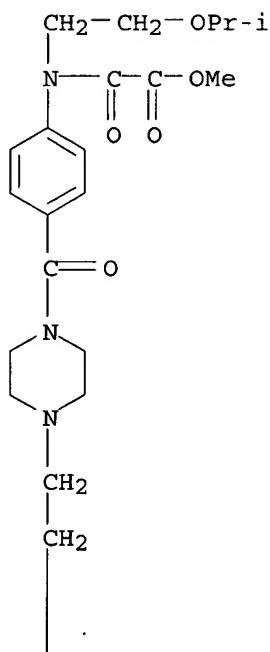
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of, as analgesic)

RN 147131-48-4 HCAPLUS

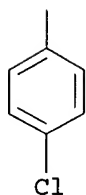
CN Acetic acid, [[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]oxo-, methyl.

ester, monohydrochloride (9CI) (CA INDEX NAME)

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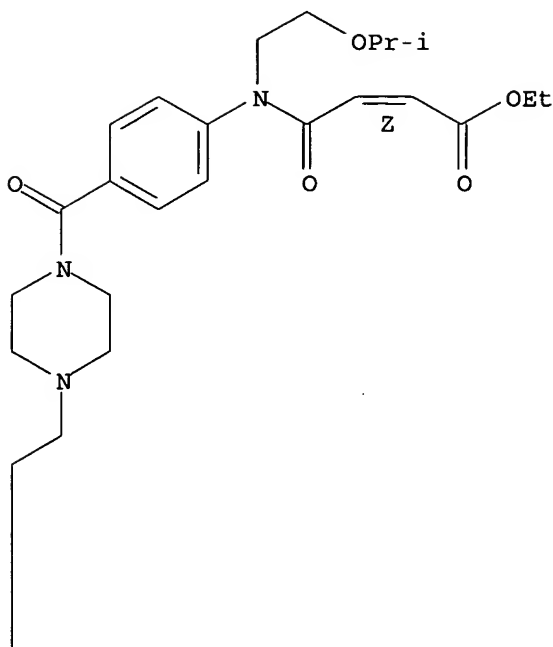


● HCl

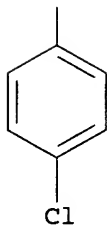
RN 147131-49-5 HCAPLUS  
 CN 2-Butenoic acid, 4-[[[4-[[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-4-oxo-, ethyl ester, monohydrochloride, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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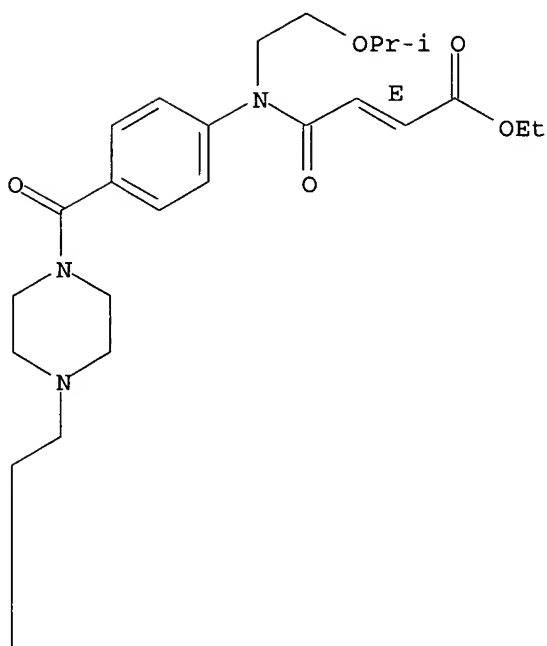


● HCl

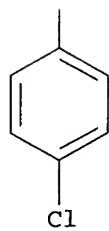
RN 147131-50-8 HCAPLUS  
 CN 2-Butenoic acid, 4-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-4-oxo-, ethyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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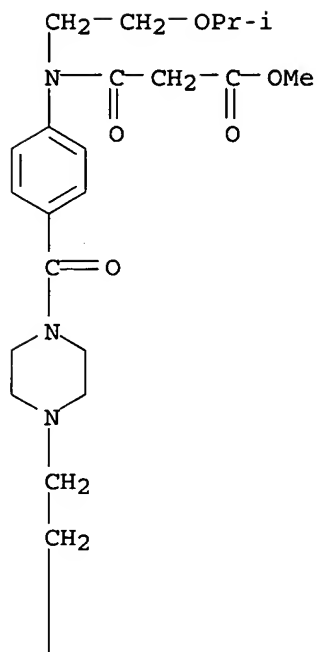
PAGE 2-A



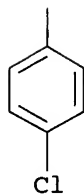
● HCl

RN 147131-53-1 HCAPLUS  
CN Propanoic acid, 3-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-3-oxo-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

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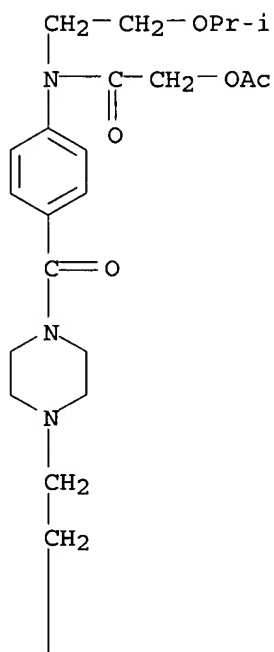
PAGE 2-A



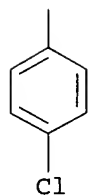
● HCl

RN 147131-54-2 · HCAPLUS  
 CN Acetamide, 2-(acetyloxy)-N-[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl]-N-[2-(1-methylethoxy)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

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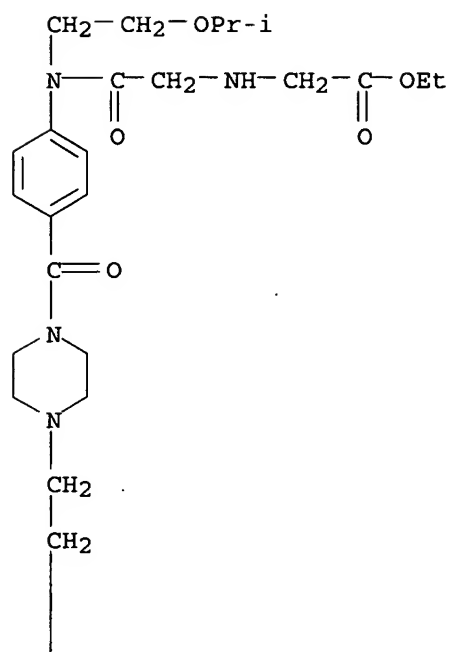
PAGE 2-A



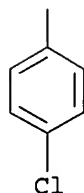
● HCl

RN 147131-61-1 HCAPLUS  
 CN Glycine, N-[2-[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-2-oxoethyl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

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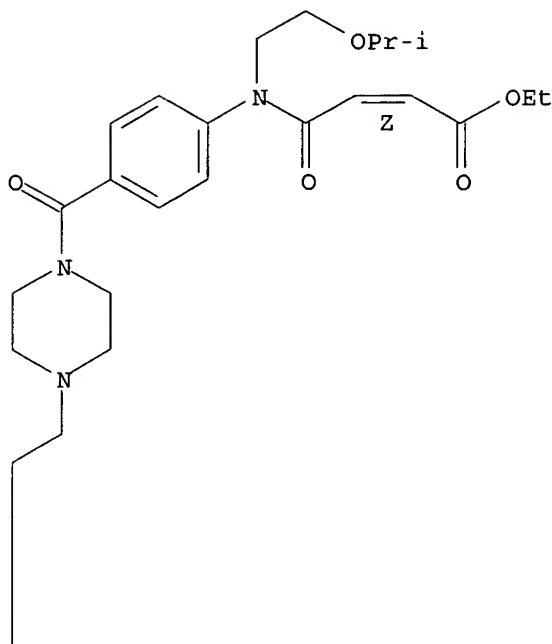


● HCl

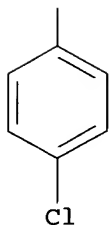
RN 147149-07-3 HCAPLUS  
 CN 2-Butenoic acid, 4-[[[4-[[4-[2-(4-chlorophenyl)ethyl]-1-piperazinyl]carbonyl]phenyl][2-(1-methylethoxy)ethyl]amino]-4-oxo-, ethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



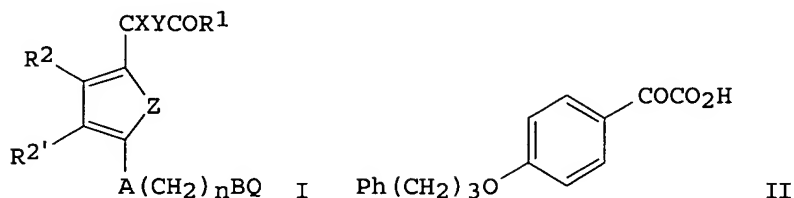
PAGE 2-A



L12 ANSWER 46 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1993:147306 HCAPLUS  
DOCUMENT NUMBER: 118:147306  
TITLE: Preparation of  $\alpha$ -oxobenzeneacetic acids and related compounds as antiischemics and antiarrhythmics  
INVENTOR(S): Guthrie, Robert William; Heathers, Guy Phillip; Higgins, Alan John; Kachensky, David Francis; Kierstead, Richard Wightmann; LeMahieu, Ronald Andrew; Mullin, John Guilfoyle, Jr.; Tilley, Jefferson Wright  
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., AG, Switz.  
SOURCE: Eur. Pat. Appl., 166 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:



PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 512352	A2	19921111	EP 1992-107135	19920427
EP 512352	A3	19930310		
EP 512352	B1	19960327		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
US 5344843	A	19940906	US 1992-850620	19920313
PRIORITY APPLN. INFO.:			US 1991-698014	A 19910509
			US 1992-850620	A 19920313
OTHER SOURCE(S):		MARPAT 118:147306		
GI				



AB Title compds. I [R<sub>1</sub> = OH, OR<sub>3</sub>, NR<sub>4</sub>R<sub>5</sub>; 1 of R<sub>4</sub>, R<sub>5</sub> = H, C<sub>1</sub>-7 (hydroxy)alkyl and the other = H, OH, C<sub>1</sub>-7 alkyl, C<sub>1</sub>-7 alkoxy; R<sub>3</sub> = (CH<sub>2</sub>CH<sub>2</sub>O)<sub>m</sub>H, CH<sub>2</sub>CHOHCH<sub>2</sub>OH, 2,2-dimethyl-1,3-dioxolan-4-yl, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, etc.; m = 1-4; R<sub>2</sub>, R<sub>2'</sub> = H, C<sub>1</sub>-7 alkyl, aryl-C<sub>1</sub>-7 alkyl, C<sub>1</sub>-7 alkoxy, OH, NH<sub>2</sub>, C<sub>1</sub>-7 alkylamino, cyano, halo, SH, etc.; A = bond, O, NR<sub>7</sub>, S, SO, SO<sub>2</sub>, C.tplbond.C, CH:CH, CH<sub>2</sub>CH, NR<sub>8</sub>CO, CONR<sub>9</sub>; R<sub>7</sub> = H, C<sub>1</sub>-7 alkyl, acyl; R<sub>8</sub>, R<sub>9</sub> = H, C<sub>1</sub>-7 alkyl; n = 0-10; B = bond, groups defined for A, CO, CS, (OCH<sub>2</sub>CH<sub>2</sub>)<sub>m</sub>O, etc.; Z = O, S, CR<sub>2</sub>:CR<sub>2'</sub>, N:CR<sub>2</sub>, CR<sub>2</sub>:N, NR<sub>11</sub>; R<sub>11</sub> = H, C<sub>1</sub>-7 alkyl; XY = O, S, :NOH, alkoxyimino, alkenyloxyimino, hydrazono, etc., or individually 1 of X and Y = halo and the other = H, halo, C<sub>1</sub>-7 alkyl, aryl-C<sub>1</sub>-7 alkyl; other possibilities for X and Y; Q = cycloalkyl, aryl, heterocyclyl; with provisos] were prepared as drugs to prevent injury to ischemic tissue and arrhythmias during and after a myocardial infarction. Thus, Me 4-hydroxy- $\alpha$ -oxobenzeneacetate in DMF containing NaH was O-alkylated by Ph(CH<sub>2</sub>)<sub>3</sub>Br and the resultant product was hydrolyzed by NaOH in MeOH to give title compound II. II had IC<sub>50</sub> of 0.5  $\mu$ M against carnitine acyltransferase 1 in mitochondria. Over 200 I were prepared

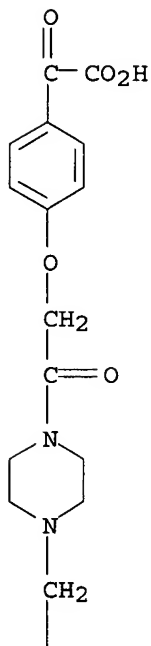
IT 146572-66-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as antiischemic and antiarrhythmic)

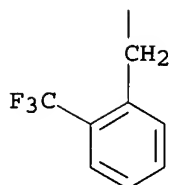
RN 146572-66-9 HCAPLUS

CN Benzeneacetic acid,  $\alpha$ -oxo-4-[2-oxo-2-[4-[2-[2-(trifluoromethyl)phenyl]ethyl]-1-piperazinyl]ethoxy]-, monohydrochloride (9CI) (CA INDEX NAME)

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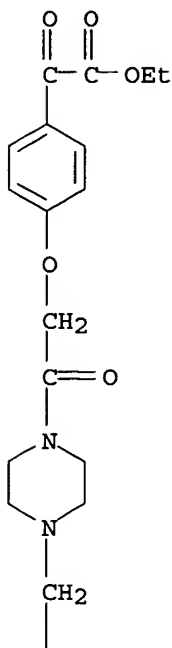
PAGE 2-A



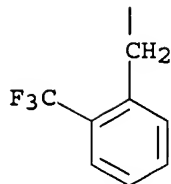
● HCl

IT 145797-87-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as intermediate for antiischemics and antiarrhythmics)  
 RN 145797-87-1 HCAPLUS  
 CN Benzeneacetic acid,  $\alpha$ -oxo-4-[2-oxo-2-[4-[2-[2-(trifluoromethyl)phenyl]ethyl]-1-piperazinyl]ethoxy]-, ethyl ester (9CI)  
 (CA INDEX NAME)

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L12 ANSWER 47 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1992:265507 HCAPLUS  
DOCUMENT NUMBER: 116:265507  
TITLE: Silver halide photographic image-forming method by development  
INVENTOR(S): Ohashi, Minoru; Koga, Masao  
PATENT ASSIGNEE(S): Mitsubishi Paper Mills, Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04016938	A2	19920121	JP 1990-121747	19900511
US 5212045	A	19930518	US 1991-697439	19910509

PRIORITY APPLN. INFO.:

JP 1990-120279

A 19900509

JP 1990-121747

A 19900511

OTHER SOURCE(S):

MARPAT 116:265507

AB Images are formed by developing a photog. material in the presence of  $R_1R_2N(CO)_2(NH)_2Z_1NHCOZnCONHZ_2(NH)_2(CO)_2NR_3R_4$  (Z = divalent linking group; Z1-2 = aromatic group; R1-4 = H, alkyl, aryl, heterocyclic group; R1R2 or R3R4 may form ring; n = 0, 1). The obtained images showed stable sensitivity.

IT 141797-72-0

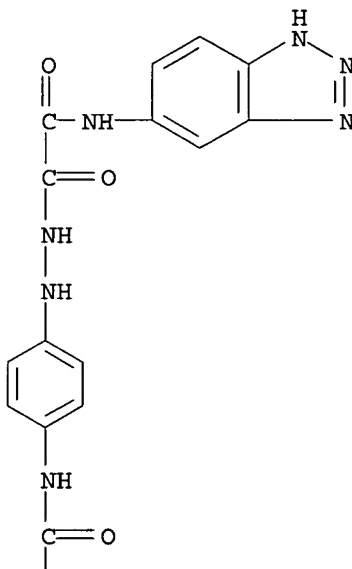
RL: USES (Uses)

(silver halide photog. development with, for stable sensitivity)

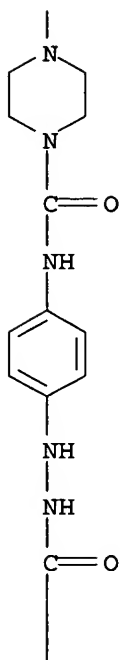
RN 141797-72-0 HCAPLUS

CN Acetic acid, (1H-benzotriazol-5-ylamino)oxo-, 2,2'-[1,4-piperazinediylbis(carbonylimino-4,1-phenylene)]dihydrazide (9CI) (CA INDEX NAME)

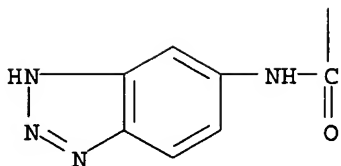
PAGE 1-A



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L12 ANSWER 48 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:408729 HCAPLUS

DOCUMENT NUMBER: 115:8729

TITLE: Novel 1,4-dihydropyridine calcium antagonists. II.  
Synthesis and antihypertensive activity of  
3-[4-(substituted amino)phenylalkyl] ester derivatives

AUTHOR(S): Ashimori, Atsuyuki; Ono, Taizo; Inoue, Yoshihisa;  
Morimoto, Satoshi; Eda, Masahiro; Uchida, Takeshi;  
Ohtaki, Yutaka; Fujino, Yoshiyuki; Kido, Hideaki; et  
al.

CORPORATE SOURCE: Res. Div., Green Cross Corp., Hirakata, 573, Japan

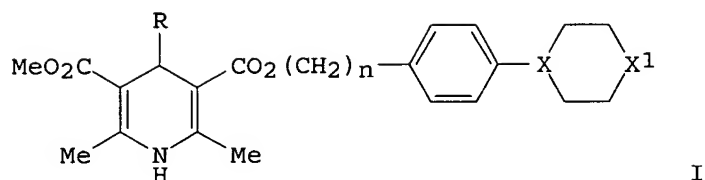
SOURCE: Chemical & Pharmaceutical Bulletin (1991), 39(1), 91-9  
CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 115:8729

GI



AB Novel 1,4-dihydropyridine derivs. bearing 3-[4-(substituted amino)phenylalkyl] ester side chains were prepared by several routes and tested for antihypertensive activity in spontaneously hypertensive rats. Most compds. showed a more potent antihypertensive effect and a longer duration of action than nicardipine. The derivs. with a benzhydrylpiperazinyl and a benzhydrylpiperidinyll group were distinctive. [(Benzhydrylpiperazinyl)phenyl]alkyl and [(benzhydrylpiperidinyll)phenyl]alkyl dihydrodimethylpyridinedicarboxylates I (R = 3-O2NC6H4, X = N, X1 = NCHPh2, n = 2; R = 4-cyano-2-pyridyl, X = N, X1 = NCHPh2, n = 2; R = 3-O2NC6H4, X = N, X1 = NCHPh2, n = 3; R = 3-O2NC6H4, X = N, X1 = CHCHPh2, X = CH, X1 = NCHPh2, n = 2) were selected as candidates for further pharmacol. investigations.

IT 134392-10-2P

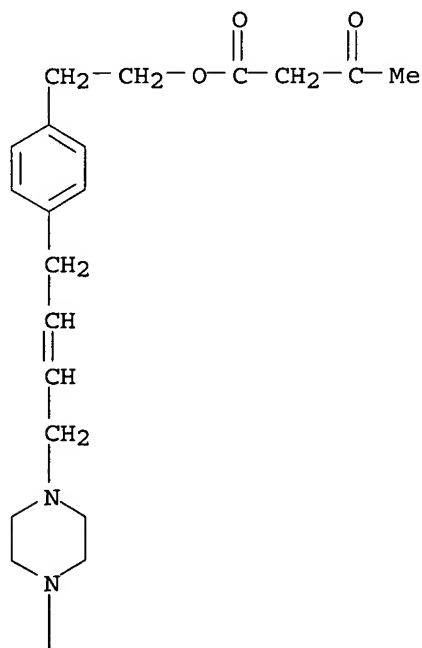
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and cyclocondensation of, with nitrobenzaldehyde and aminocrotonate)

RN 134392-10-2 HCAPLUS

CN Butanoic acid, 3-oxo-, 2-[4-[4-[4-(diphenylmethyl)-1-piperazinyl]-2-butenyl]phenyl]ethyl ester (9CI) (CA INDEX NAME)

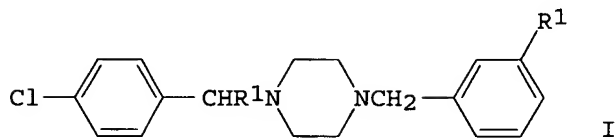
PAGE 1-A



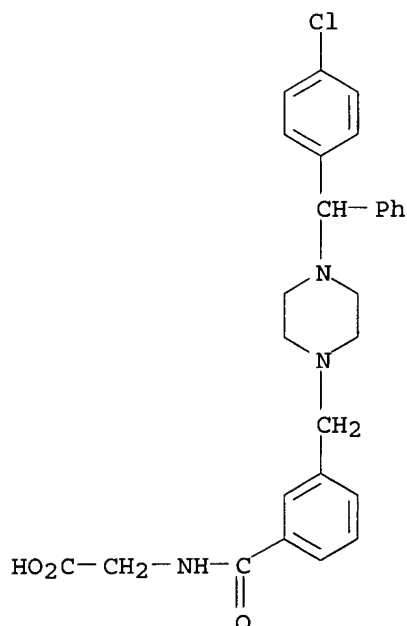
PAGE 2-A

|  
CHPh<sub>2</sub>

L12 ANSWER 49 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1989:515140 HCAPLUS  
DOCUMENT NUMBER: 111:115140  
TITLE: Synthesis of some metabolites of meclozine  
AUTHOR(S): Goenechea, Sabino; Brzezinka, Harald; Glanzmann,  
Gerda; Ruecker, Gerhard; Neugebauer, Michael  
CORPORATE SOURCE: Inst. Rechtsmed., Univ. Bonn, Bonn, D-5300/1, Fed.  
Rep. Ger.  
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1989),  
322(6), 355-7  
CODEN: ARPMAS; ISSN: 0365-6233  
DOCUMENT TYPE: Journal  
LANGUAGE: German  
OTHER SOURCE(S): CASREACT 111:115140  
GI



AB The meclozine (I, R = Ph, R1 = Me) metabolites I [R = Ph, R1 = CO<sub>2</sub>H, CONH<sub>2</sub>, CONHCH<sub>2</sub>CH<sub>2</sub>SO<sub>3</sub>H; R = 3,4-MeO(HO)C<sub>6</sub>H<sub>3</sub>, R1 = CO<sub>2</sub>H] and the mono- and di-N-oxides of I (R = Ph, R1 = Me) were prepared  
IT 122504-58-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 122504-58-9 HCAPLUS  
CN Glycine, N-[3-[[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]methyl]benzoyl]- (9CI) (CA INDEX NAME)



L12 ANSWER 50 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:95277 HCAPLUS

DOCUMENT NUMBER: 110:95277

TITLE: Preparation of pyridazinone derivatives as  
cardiotonics

INVENTOR(S): Okujima, Hiromi; Narimatsu, Akihiro; Kobayashi, Makio;  
Furuya, Rikizo; Kitada, Yoshi

PATENT ASSIGNEE(S): Mitsubishi Kasei Corp., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

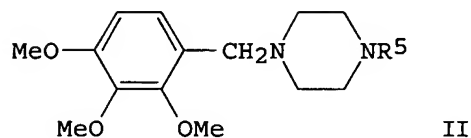
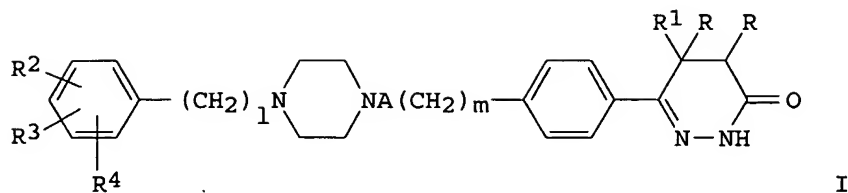
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63218666	A2	19880912	JP 1987-53643	19870309
PRIORITY APPLN. INFO.:			JP 1987-53643	19870309
OTHER SOURCE(S):	MARPAT	110:95277		
GI				





AB Title compds. I [R = H or RR = bond; R1 = H, C1-5 alkyl; R2, R3, R4 = H, C1-5 alkoxy, OH; R2R3, R3, R4, R2R4 = OCH2O, O(CH2)2O; A = bond, (CH2)nNH; l = 0-4; m,n = 1-4] are prepared A solution of p-(BrCH2)C6H4CO(CH2)2CO2Me in MeOH was refluxed with a piperazine II (R5) for 8 h to give 52% II [R5 = CH2C6H4[[CO(CH2)2CO2Me]-p], and the latter and 80% H2NNH2 in AcOH were refluxed for 1 h to give 51% I (R = R1 = H; R2 = 2-MeO; R3 = 3-MeO; R4 = 4-MeO; A = bond) (III), which was converted to its HCl salt. III.HCl showed, in vitro, at 3 + 10<sup>-5</sup> g/mL, 35.3% increase of muscular contraction in guinea pigs left atrium and at 100 µg 16.5% increase of dog-niple muscular contraction.

IT 119115-71-8P 119115-74-1P 119115-75-2P

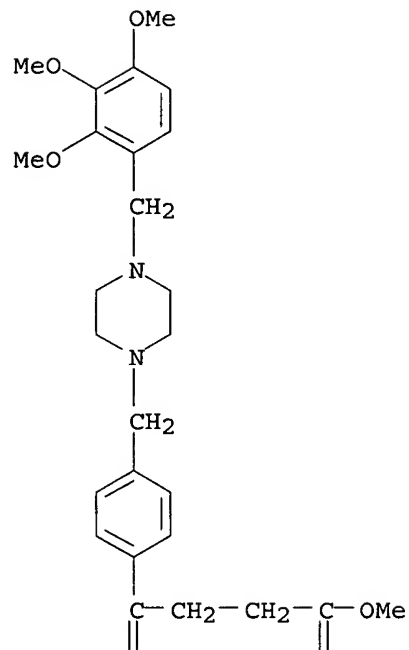
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of pyridazinone cardiotonics)

RN 119115-71-8 HCAPLUS

CN Benzenebutanoic acid, γ-oxo-4-[[4-[(2,3,4-trimethoxyphenyl)methyl]-1-piperazinyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

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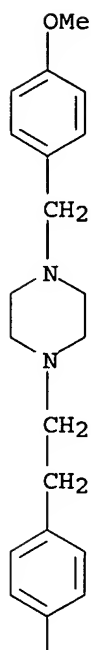


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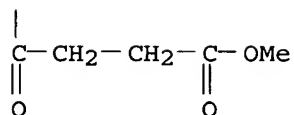


RN 119115-74-1 HCAPLUS  
 CN Benzenebutanoic acid, 4-[2-[4-[(4-methoxyphenyl)methyl]-1-piperazinyl]ethyl]-gamma-oxo-, methyl ester (9CI) (CA INDEX NAME)

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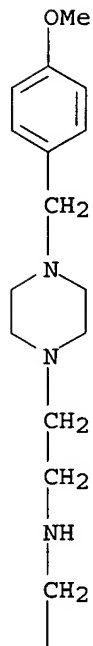


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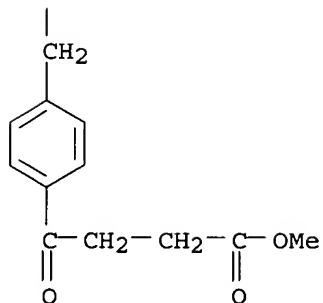


RN 119115-75-2 HCAPLUS  
 CN Benzenebutanoic acid, 4-[2-[[2-[4-[(4-methoxyphenyl)methyl]-1-piperazinyl]ethyl]amino]ethyl]-γ-oxo-, methyl ester (9CI) (CA INDEX NAME)

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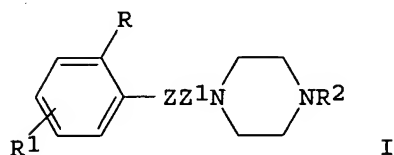


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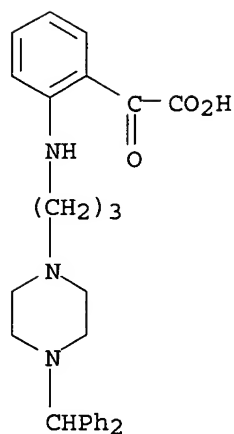


L12 ANSWER 51 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1981:550706 HCAPLUS  
DOCUMENT NUMBER: 95:150706  
TITLE: Piperazine derivative, processes for the preparation thereof, and pharmaceutical composition comprising the same  
INVENTOR(S): Teraji, Tsutomu; Oku, Teruo; Namiki, Takayuki  
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan  
SOURCE: Brit. UK Pat. Appl., 14 pp.  
CODEN: BAXXDU  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2056968	A	19810325	GB 1979-29092	19790821
JP 56032474	A2	19810401	JP 1980-115296	19800820
PRIORITY APPLN. INFO.: GI			GB 1979-29092	A 19790821



- AB Piperazines I [R = CO<sub>2</sub>H, CO<sub>2</sub>H derivative, acylamino; R<sub>1</sub> = H, halo, alkyl, alkoxy, aryl, acylamino; R<sub>2</sub> = aralkyl; Z = NR<sub>3</sub>, O, S, NHCO (R<sub>3</sub> = H, acyl); Z<sub>1</sub> = alkylene], and their pharmaceutically acceptable salts, having antiallergic activity, were prepared E. g., a solution of
- 1-[3-(4-benzhydryl-1-piperazinyl)propyl]isatin in N aqueous NaOH and THF was treated by dropwise addition of 15% aqueous H<sub>2</sub>O<sub>2</sub> at room temperature and the mixture was stirred 5 h at 70°, cooled to room temperature, treated with Na<sub>2</sub>SO<sub>3</sub> (pH 1, 10% HCl), diluted with EtOAc, adjusted to pH 9 (aqueous NaHCO<sub>3</sub>), and stirred 0.5 h to give
- I [R = CO<sub>2</sub>H, R<sub>1</sub> = H, R<sub>2</sub> = CHPh<sub>2</sub>, Z = NH, Z<sub>1</sub> = (CH<sub>2</sub>)<sub>3</sub>] (II). A 10 mg/kg p.o. dose of II produced complete inhibition of anaphylactic asthma in guinea pigs.
- IT **79310-58-0P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of, as allergy inhibitor)
- RN 79310-58-0 HCAPLUS
- CN Benzeneacetic acid, 2-[[3-[4-(diphenylmethyl)-1-piperazinyl]propyl]amino]-α-oxo-, monosodium salt (9CI) (CA INDEX NAME)



● Na

L12 ANSWER 52 OF 52 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1979:466263 HCAPLUS

DOCUMENT NUMBER: 91:66263

TITLE: Silver halide color photographic yellow couplers

INVENTOR(S): Yamashita, Kiyoshi; Kawakatsu, Tetsu; Nakaya, Mamoru

PATENT ASSIGNEE(S): Mitsubishi Paper Mills, Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

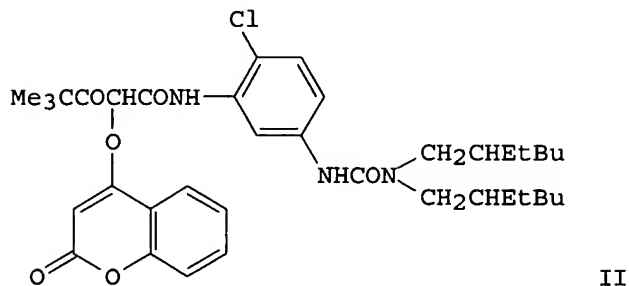
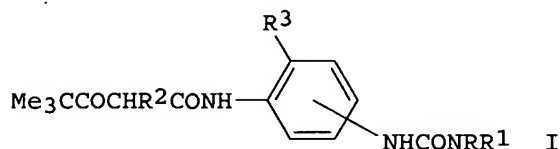
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 54023528	A2	19790222	JP 1977-88606	19770723
JP 56007221	B4	19810217		
PRIORITY APPLN. INFO.:			JP 1977-88606	A 19770723
GI				



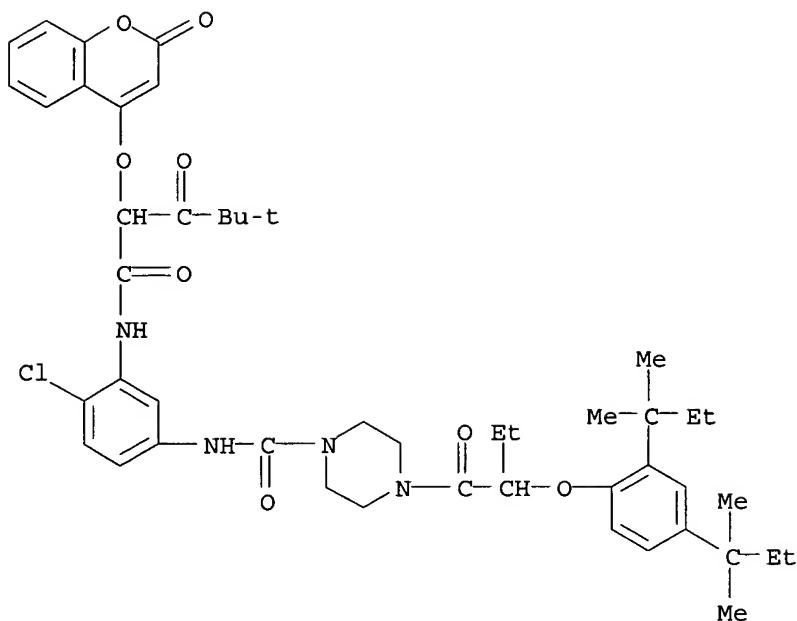
AB Ag halide photog. yellow couplers of the general formula I (R, R1 = alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, substituted aralkyl, aryl, substituted aryl; R2 = H or a group released during the color development; R3 = H, halo, alkyl, alkoxy; the NHCONRR1 group is attached to 4 or 5 position of the anilide ring) are claimed. Thus, the yellow coupler II 4 + 10<sup>-3</sup> mol was added to a Ag(Br,Cl) emulsion containing 8 + 10<sup>-2</sup> mol Ag halide, and the emulsion was coated on a film support. The film was sensitometrically exposed and developed to give D<sub>max</sub> and λ<sub>max</sub> of 2.38 and 439 nm, resp.

IT 70945-79-8

RL: TEM (Technical or engineered material use); USES (Uses)  
(photog. yellow coupler)

RN 70945-79-8 HCAPLUS

CN 1-Piperazinecarboxamide, 4-[2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-1-oxobutyl]-N-[4-chloro-3-[[4,4-dimethyl-1,3-dioxo-2-[(2-oxo-2H-1-benzopyran-4-yl)oxy]pentyl]amino]phenyl]- (9CI) (CA INDEX NAME)



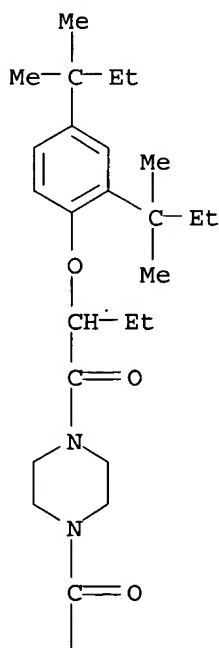
IT 70945-81-2

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with sulfonyl chloride)

RN 70945-81-2 HCAPLUS

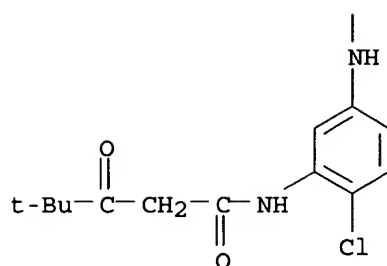
CN 1-Piperazinecarboxamide, 4-[2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-1-oxobutyl]-N-[4-chloro-3-[(4,4-dimethyl-1,3-dioxopentyl)amino]phenyl]-(9CI) (CA INDEX NAME)

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